# Application of the LigaSure™ tissue sealing system to intestinal resection.

## Experimental and clinical trial

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**Application of the LigaSure™ tissue sealing system to intestinal resection. Experimental and clinical trial**

AIM: *To evaluate the efficacy and safety of applying the LigaSure™ system (approved for vessel sealing) to intestine sealing procedures.*
METHODS: *Fifteen New Zealand rabbits underwent laparotomic intestinal resection of the cecum (7 animals, group 1) or small intestine (8 animals, group 2), sealing the stumps by applying precisely controlled electrothermal energy and physical pressure in an experimental setting. The tightness of these seals was tested immediately after completing the surgical procedure and subsequently at autoptic investigation. The effectiveness of the sealing action was also assessed on biological samples of human duodenum and appendix. All seal zones were the object of histopathological study with a view to assessing the effect of applying the system to human and animal tissues.*
RESULTS: *All the stumps appeared to be sealed immediately after the application of the instrument. Postoperatively, 28 rabbit intestine stumps were effectively investigated: 10 (belonging to the first experimental group) were found still open and 18 (belonging to the second group) were sealed. The effectiveness of the seal was progressively optimized by adjusting the technique adopted in using the instrument. The area of the seal has the appearance of a homogeneous eosinophilic band with a few necrobiotic cells. An inflammatory process develops with a stromal reaction and the formation of connective tissue indistinguishable from the manual sutures. Already after 12 days, the area of the seal was no longer identifiable.*
CONCLUSIONS: *The application seems to be effective, though further experimental studies are needed to validate the effectiveness and safety of the LigaSure™ system in sealing the intestine.*

KEY WORDS: Animal study, Bipolar electrocoagulation, Dehiscence, Healing process, Intestinal resection, LigaSure™ device, Radiofrequency, Seal zone, Side-to-side anastomosis, Suture.

## Introduction

Surgery has recently made a prodigious amount of progress thanks to the contribution of devices using increasingly sophisticated technologies. While some tools have been abundantly tried and tested (mechanical suturing devices, biofragmentable anastomosis ring (BAR-Valtrac), etc.), others are still in the experimental stages, such as fibrin sealants, compression anastomosis clips (CAC), biologically adsorbable membranes, and so on. Among the latter, there is also the LigaSure™ tissue sealing system used in human surgery for vessel sealing in patients undergoing open gynecologic procedures, urologic and bowel surgery – a usage for which it was approved by the American Food and Drug Administration in 1999 [1-3]. Animal studies have shown that bipolar electrocoagulation with the LigaSure™ system is safe for sealing vessels (arteries and veins) up to 7 mm in diameter [4-7]. Degenerative changes after electrocoagulation are localized and only spread up to 2 mm from the area where the instrument is applied.
The LigaSure™ vessel sealing system has not hitherto been used to seal intestines.
Our study proposes to add an experimental contribution to help ascertain the feasibility of extending the use of LigaSure™ to intestinal sealing procedures.

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## Materials and methods

Subject to the approval of, and subsequent supervision by the University's Central Veterinary Services, we applied the instrument to rabbit intestine during intestinal resection surgery. The study included 15 New Zealand white rabbits (reared under semi-barrier conditions), 7 weighing 5 kg in the first group and 8 weighing 2.8-3 kg in the second group. One or two days before surgery, the animals were placed on a water diet and given antibiotic prophylaxis with cefazolin (Cefamezin®; Pharmacia & Upjohn, Milan, Italy) 250 mg x 2/day im. On the day of surgery, they were premedicated with an iv. injection of a solution of xylazine (a sedative, muscle-relaxing and analgesic medication for veterinary use – Rompun®; Bayer, Leverkusen, Germany) 5-8 mg/kg iv. and ketamine hydrochloride (Ketanest®, Pfizer, New York, USA) 30-40 mg/kg iv. Anesthesia was induced and maintained with propofol (Diprivan®; AstraZeneca, Milan, Italy) 5-14 mg/kg iv. The animals underwent resection of the cecum or small intestine, using the LigaSure™ vessel sealing system (Valleylab, Boulder, Colorado, USA) to close the intestinal loops, using the vessel coagulation instrument with a standard disposable electrode and standard handset in 10 cases, and with the Max electrode and handset in 5. Five instruments were used in all: the Std for cases No. 1 to 6, the Max for case No. 7, the Std for cases No. 8 to 11, the Max for cases No. 12 to 14, and the Max for case No. 15. The first 7 rabbits underwent surgery of the cecum (group 1) while the other 8 had small intestine resection (group 2). In the first group, only one seal zone was created by means of two applications, the first on the mesentery side, the second on the opposite side to complete the closure of the loop, and the seal was cut in half. In the second group, two seal zones were obtained, each created with two applications adjacent applications in order to widen the seal. Figures 1 and 2 illustrate the method used to apply the LigaSure™ system in the first and second groups, respectively. In the second group, the surgeons were able to use microsurgical tools.

The protocol involved hydration with glucose solution alone on the first and second postoperative days and a return to a normal diet with animal feed on the third. For 4 days the animals were given antibiotic therapy with cefazolin 250 mg x 2/day im. and pain was controlled with phenylbutazone (Fenilbutazone 20%; Farmaceutici Gellini, Latina, Italy) 10-25 mg/kg im. The animals were to be suppressed on or near the 12$^{th}$ postoperative day to evaluate the short-term outcome of the application. The treated section of loop was accurately studied at autopsy to assess its global conditions, then removed and fixed for histological examination. Microscopic investigations were conducted on specimens stained with hematoxylin & eosin.

The LigaSure™ Max was also applied to segments of duodenum and appendix suitably selected from human biological samples during duodenal resection surgery and appendicectomy.

## Results

The instrument is easy to use and, once it has been prepared, it takes effect without any further action on the part of the surgeon. We were able to visually evaluate the effect of the LigaSure™ sealing system on the intestinal tissue during the procedure: the seal zone had the appearance of a white band that became transparent in places; the seal on the loop seemed to be complete. Macroscopically, the zone appeared to withstand manipulation and had an elastic consistency; there were no signs of bleeding or leakage of intestinal contents through the seal. There was evidence of a minimal lateral thermal diffusion, starting from the margins of the jaws on the handset holding the electrode. It was only after the repeated use of the electrode that this phenomenon expanded up to 3-4 mm wide, with the appearance of an irregular whitening of the tissue on either side of the jaws. The sealed tissue did not adhere to the electrode, there was no apparent damage to the surrounding tissues, nor any signs of sparks and the combustion fumes were practically nil. The LigaSure™ was quick to apply and the sealing cycle took only a few seconds. There was no intraoperative bleeding at the seal, while some bleeding was caused during the manual preparation of the anastomosis.

Intraoperative complications occurred in animals No. 2 and 6. At the end of the operation on case No. 2, the seal on one stump partially reopened while it was being manipulated to replace it in the abdomen, requiring a redo sealing procedure and a suture with thread on the open stump. In case No. 6, we attempted to prepare the intestinal anastomosis using the LigaSure™ instrument in the same way as a mechanical linear suturing device. The jaws were easy to place in position and the system was started, but when the sealing cycle was complete the electrode was found stuck to the tissue. When an attempt was made to detach it manually, pulling the instrument's jaws open caused a rupture in the loop and a consequent spillage of fecal material in the abdomen. This animal was consequently excluded from the study, while only one stump was considered for case No. 2.

In the postoperative period, 28 stumps were effectively analyzed (Table 1). We were only able to evaluate the outcome of the application around the 12$^{th}$ day in 3 cases (No. 4, 12 and 13), while postoperative complications made it necessary to proceed sooner with the autopsy in the others.

In all, 18 stumps were sealed and 10 were open. To be more precise, of the 12 stumps analyzed in the first group, 8 were open and 4 were closed; of the 16 considered in the second group, 2 were open and 14 were closed.

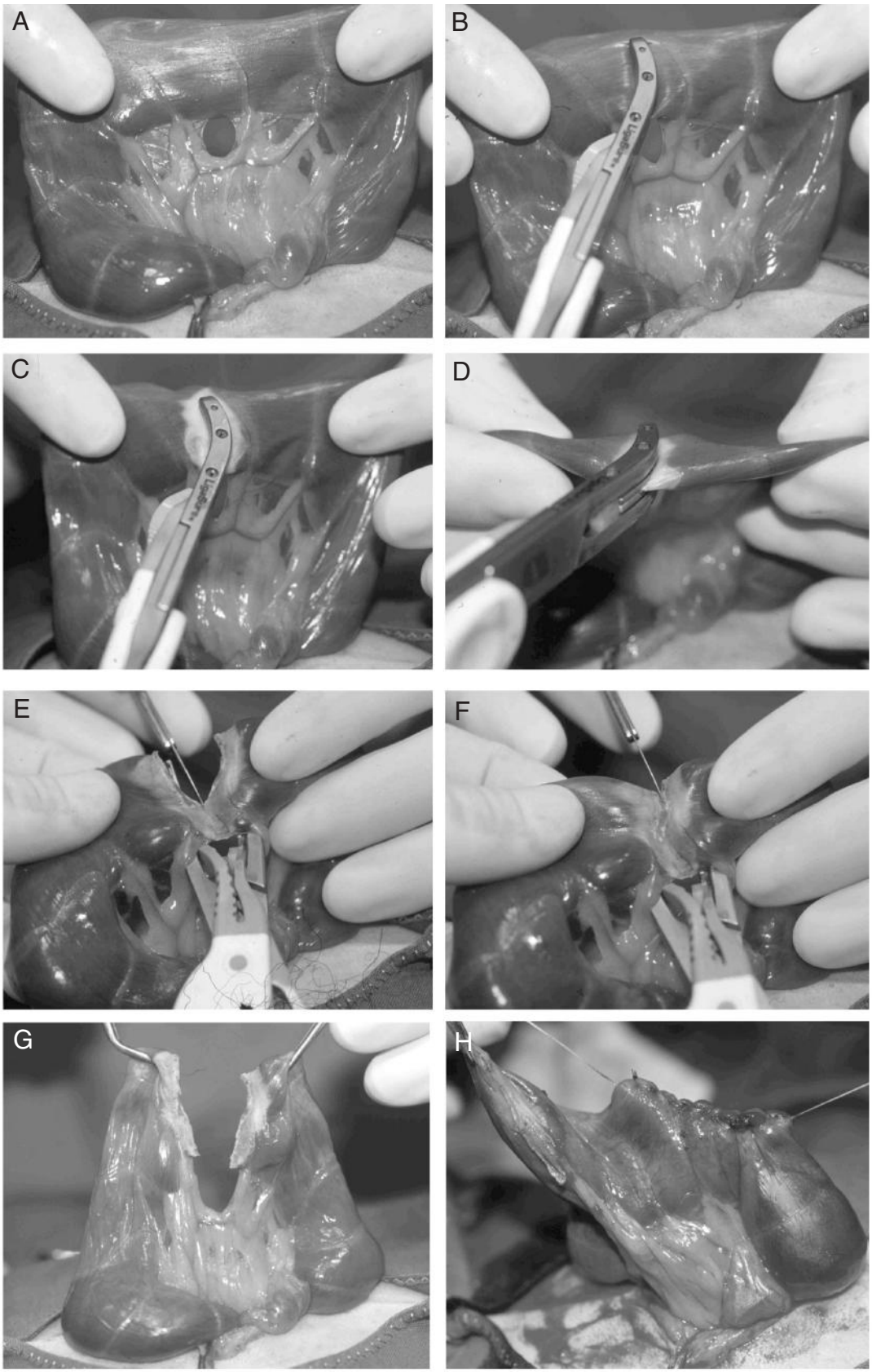


**Fig. 1:** *Intraoperative specimen.* The LigaSure™ tissue sealing system applied to a loop of cecum in the first group of animals. **A**. the loop of cecum is isolated. **B**. the LigaSure™ instrument placed around the loop of cecum. **C**. the LigaSure™ in action on the loop of cecum; the whitened appearance on either side is due to lateral thermal diffusion. **D**. side view of thermal diffusion. **E, F**. section of loop at center of seal zone. **G**. two intestinal stumps sealed with the LigaSure™. **H**. intestinal stump sealed with the LigaSure™ and adjacent anastomosis.

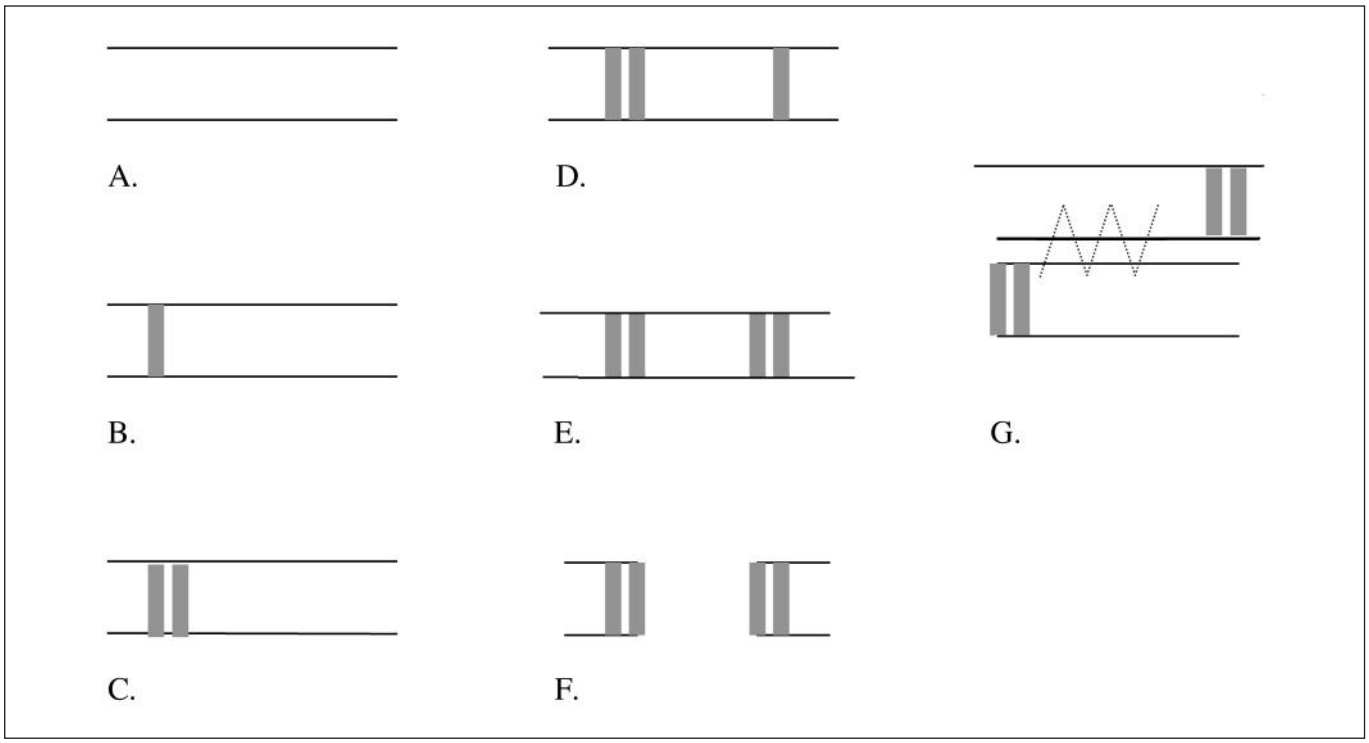


**Fig. 2:** Schematic representation of the method used to apply the LigaSure™ sealing system in the second group. **A**. the isolated loop of small intestine. **B**. first application on first stump. **C**. second application on first stump. **D**. third application on second stump. **E**. fourth application on second stump. **F**. section of loop between second and fourth applications. **G**. intestinal continuity restored with a side-to-side anastomosis.

One stump belonging to case No. 2 leaked from one corner of the seal when tested with physiological solution. The instrument had not completely clinched one corner of the stump. The same situation was found in case No. 8, where the corner had been damaged by a stitch inserted for the anastomosis, which was closely adjacent to the seal zone. Case No. 9 had a fistula between the operated area and the stretch of loop upstream, but histological examination ruled out the possibility of this complication influencing the seal zone.
Autopsy on cases No. 4, 12 and 13 (which demonstrated an optimal clinical course) revealed adhesions incorporating the seal zone and the area of the anastomosis: the seal zone resulting from the application of the LigaSure™ was grossly difficult to distinguish from the tissue sutured with thread. Under the microscope, the electrocoagulated tissue had the general appearance of a homogeneous eosinophilic band with a few necrobiotic cells and no signs of hemorrhage. We found that the seal zone goes through an inflammatory process, progressively reabsorbing the necrotic material and developing a stromal reaction with the formation of connective tissue which replaces the necrotic tissue.
The application of the system to human tissue specimens produced a perfect sealing action on the walls, with no bleeding or leakage of intestinal contents from the seal zone.

## Discussion

Our study aimed to assess the effect of applying the LigaSure™ sealing system to intestinal tissue to evalu-

TABLE I - *Autoptic findings on the intestinal stumps with the LigaSure™ seal zone.*

| Stumps | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Open** | | **Closed** | | **Damaged*** | | **Valid†** | |
| **1st** | **2nd** | **1st** | **2nd** | **1st** | **2nd** | **1st** | **2nd** |
| 1 | 1 | 4 | 4 | 2 | 2 | 6‡ | 6‡ |
| 3 | 3 | 12 | 12 | *8* | | 7 | 7 |
| 5 | 5 | 13 | 13 | | | | *8* |
| *14* | | | | | | 9 | 9 |
| | | | | | | 10 | 10 |
| | | | | | | 11 | 11 |
| | | | | | | | *14* |
| | | | | | | 15 | 15 |

**Key: 1st**: proximal stump. **2nd**: distal stump.
***Damaged**: complications occurred in seal zone on stump.
†**Valid**: any complications were outside the seal zone. Cases No. 7 and 14: hemorrhagic intestinal necrosis. Cases No. 8, 9, 10, 11: intestinal occlusion. Case No. 15: intestinal infarction.
‡6: the damage was caused by what turned out to be an improper use of the instrument.

ate the feasibility of its use in intestinal resection surgery as an alternative to mechanical or manual sutures. The technique we adopted in the first group proved unsuitable. The seal zone obtained with a single application proved to "too narrow" to ensure the dieresis on both sides and thus obtain a reliable seal on both stumps. We consequently used two adjacent applications, which proved more effective in sealing both stumps. We also switched from the cecum to the small intestine because the former was judged unsuitable because of its diameter and because its resection had an excessive fallout on the function of a stretch of the intestinal tract that proved fundamental to the rodent's survival. These changes enabled us to obtain more encouraging results. The stumps were sealed and adequate in virtually all the subsequently treated cases and their mean survival improved from 3 days in the first group to 4.5 days for the first cases in the second group (subgroup A: cases No. 8-11) and 7 days for the remainder of the second group (subgroup B: cases No. 12-15). The stumps of the cases in subgroup A were found intact despite the early death of the animals due to intestinal occlusion, related to a stenosis of the manually-prepared anastomosis and consequently could not be attributed to the LigaSure™ seal. In the light of this experience, the complication was avoided in subgroup B by expanding the mouth of the anastomosis. The use of microsurgical instruments in this subgroup also proved particularly helpful.

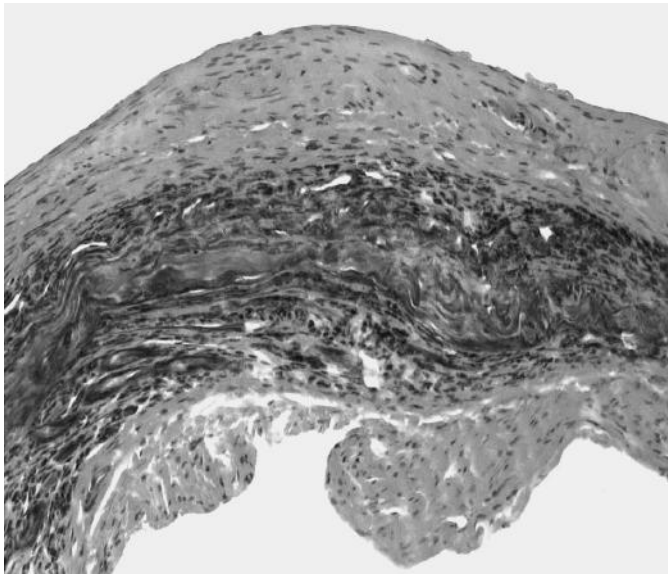

Fig. 3: *Histology of the seal zone.* Band of coarctation of the intestine, showing central hematoxylinophilic stria, epithelial and lymph cell elements around the lumen and homogenization of the surrounding mesenchymal component.

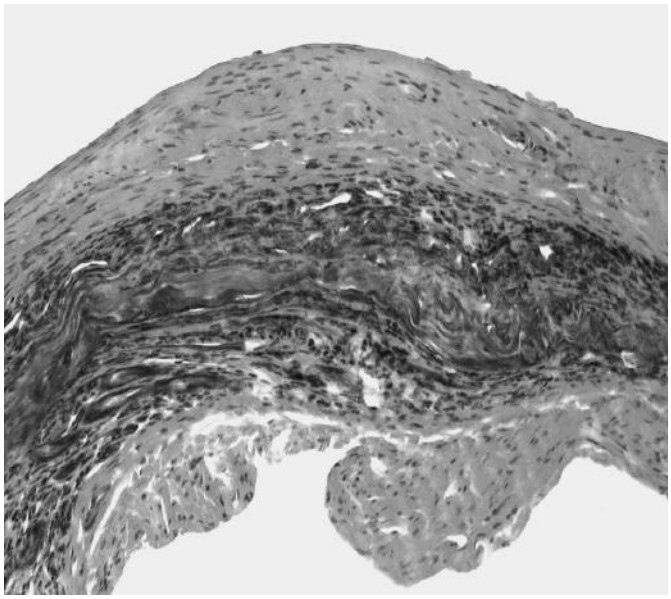

Fig. 4: *Seal zone histology.* Sealed intestine with the treated zone showing a central hematoxylinophilic band, atrophy of the leiomuscular component, and homogenization and fibrosis of the wall.

The LigaSure™ instruments are disposable, i.e. they are designed for use in a single surgical procedure, but in our experimental setting they were used for more than one animal. The problems relating to the closing and opening of the jaws could have been avoided by using new electrodes for each surgical procedure, so it would seem essential to use each LigaSure™ instrument only once.

From the histopathological standpoint, the seal zone was initially characterized by a band of intestinal tissue coarctation with central hematoxylinophilic stria, epithelial and lymph cell elements around the lumen and homogenization of the surrounding mesenchymal component (figures 3 and 4). There was evidence of central necrosis in the epithelial and lymph cell components with the coagulation of the structures, recognizable cell structures and a modest inflammatory reaction. Subsequently, a granulocytic infiltrate became apparent, followed by the homogenization and fibrosis of the wall.

The inflammatory infiltrate revealed at histology had an acute abscessed component with a xanthogranulomatous organization, and was much more evident in the cases sacrificed or dying due to complications; this finding (in cases with open stumps and in those with sealed stumps) suggests that the inflammation was caused by the technical difficulties we encountered, whereas any extension of the inflammation from the tissue treated with the LigaSure™ system was ruled out.

## Conclusions

The complications that we observed were mainly attributable to technical difficulties: this was our first experience in this experimental setting, and we needed to learn from the evidence emerging at each step in the trial. Generally speaking, we found that the instrument quick-

ly and easily seals the intestinal tissue without any bleeding. The seal is intrinsic in the intestinal wall, with no need for any foreign material. The instrumentation designed for sealing vessels 7 mm in diameter is out of proportion and unsuitable for use on intestinal loops. Ideally, we need an instrument capable of sealing the loop with a single application. Further studies are needed before a final judgement can be reached on the LigaSure™ sealing system's application to intestinal resection, preferably testing it on a porcine model, the intestinal features of which are more like those of humans, in our opinion. In the animals that survived up to the endpoint in our study, there was virtually no macroscopic trace of the seal already by the 12th postoperative day, which prompts us to suggest that the seal zone needs to marked with India ink or non-absorbable stitches to facilitate the identification of the seal tissue to sample for macro- and microscopic investigation.

## Riassunto

OBIETTIVO: Valutare l'efficacia e la sicurezza di impiego sull'intestino del nuovo sistema di sintesi LigaSure™, attualmente impiegato per la coagulazione vasale.
MATERIALI E METODI: 15 conigli New Zealand sono stati sottoposti ad intervento di resezione intestinale secondo tecnica tradizionale. Si può individuare un primo gruppo di 7 campioni operati a livello di cieco e un secondo gruppo di 8 campioni operati a livello di tenue. Per chiudere l'ansa intestinale è stato usato il sistema di sintesi LigaSure™. Si è stabilito di verificare l'effetto dell'applicazione a distanza di 10-13 giorni dall'intervento.
Inoltre, un tratto di duodeno e un segmento di appendice umani sono stati opportunamente individuati da campioni biologici umani e chiusi con applicazione di LigaSure™.
RISULTATI: Nel periodo postoperatorio sono stati efficacemente indagati 28 monconi di intestino. In totale, 18 monconi erano chiusi, 10 aperti. Tre campioni hanno avuto decorso clinico ottimo e sono stati soppressi secondo protocollo in 10ª-13ª giornata. Le complicanze cliniche che si sono verificate negli altri campioni erano indipendenti dall'effetto dell'applicazione e imputabili a difficoltà tecniche intercorse.
Sull'intestino umano l'applicazione è risultata valida.
CONCLUSIONI: L'effetto dell'applicazione sembra valido. Ulteriori studi sperimentali sono necessari per convalidare l'efficacia e la sicurezza del sistema LigaSure™ sull'intestino.

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