Experimental testing of the TOP* stapler prototype

* **Tensile and Optimal Perfusion stapler**

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Introduction

Following development of the concept in '*Optimizing stapled gastro-intestinal anastomosis*', an experimental stapler was constructed for studies in pigs.

In the following experimental studies, the concept of anastomotic healing using the conventional stapler (two row concentric overlapping staple lines) is compared with the new experimental TOP stapler. The TOP stapler is identical with a conventional stapler except for the stapling mechanism. This is configured with one inner concentrically placed staple line with 3.8 mm staples bent with conventional compression force, combined with an outer staple line with radial/transversely placed 4.8 mm staples positioned at the intertwining points of the inner concentric staples and bent according to specifications, ensuring less pressure on the tissues for optimal perfusion.

In Figures 1 and 2 the orientation of the TOP staples is demonstrated.

Figure 1

Figure 2

In this document we will describe the animal experiments performed in pigs to test the functional results and make a comparison to the conventional stapler.

Animal experiments

Experiments were performed in the ARIA-AMC Amsterdam animal research centre, after approval of the Animal Ethical Commission of the University of Amsterdam, under GLP. Experiments were performed by A.P.J. Houdijk, MD, PhD, oncologic Gastro-Intestinal Surgeon and F.J.T. van Oosterom, MD, PhD, Plastic and Reconstructive Surgeon.

First experiment: testing of the animal model with conventional stapler

In 2014, experimental set-up and anastomotic healing was studied in pigs, using a standard conventional CEEA 28 mm stapler. The study and set-up of Wenger c.s.[1] was used as a guideline and reference.

In 4 pigs (no. 1,2,3,4), weighing 40; 39; 61; 61 kg respectively a low median laparotomy was performed and a colonic STS anastomosis was performed, after transection of the colon using a linear conventional GIA stapler. In pig no. 1 and 2 the anastomosis was performed in the caecum, in pigs no. 3 and 4 the anastomosis was performed in the descending colon.

After 7 days, a second laparotomy was planned and the anastomoses were assessed clinically.

The clinical post-operative course was uneventful.
During re-operation the following observations were made:

- Pig 1: no adhesions. Mucosal lining continuous, local hyperemia and loose staples and localised necrosis intra-luminal at the level of the anastomosis, as seen in *Figure 3*.

Figure 3

- Pig 2: extensive adhesions of the liver, parietal peritoneum, and colon, covering a perforation of the anastomosis. The anastomotic serosal side outside the perforation showed minor adhesions. *Figures 4, 5* show the adhesions around the perforation and the perforation proper respectively. At the mucosal side, again necrosis of the inner staple line was seen, with loose staples intra-luminally.

- Pig 3: a small intestinal adhesion at level of anastomosis. Healing of anastomosis as first pig 1 (as described above).

- Pig 4: a few adhesions around anastomosis. Healing as described above for pig 1.

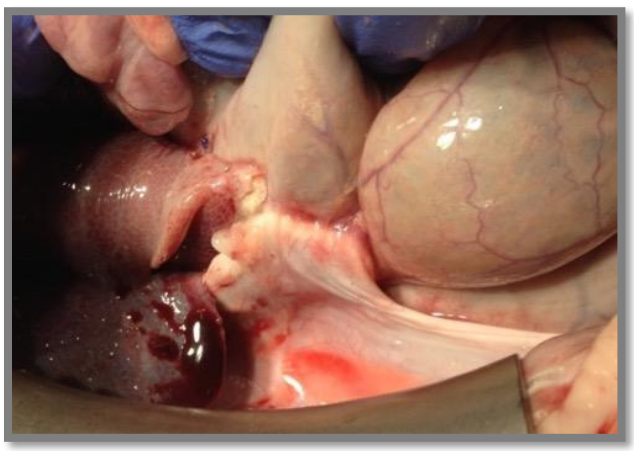

Figure 4

Figure 5

Second experiment: experimental healing of the TOP stapler
The animal experiments with the TOP stapler were planned after the prototype had been tested for staple function on cadaver pig gut segments and human fresh gut segments.

In December 2016 the function of the TOP stapler prototype was tested. The purpose of this experiment was to study clinical intestinal anastomotic healing after 7 days. Two pigs were used in this experiment.

In the first pig (no. 5), weighing 80 kg, a side to side anastomosis was created in the sigmoid colon with the TOP stapler after the gut was divided with a conventional GIA stapler. *Figure 6* shows that the transverse staples approximate the gut segments with little tension.

Figure 6

Due to small serosal damage a PDS stitch was placed near the anastomosis. The postoperative course was uneventful. The pig was sacrificed after 7 days. There were remarkably little adhesions inside the abdomen. The only adhesion that was found was formed between a GIA staple line and the left fallopian tube (see *Figure 7*).

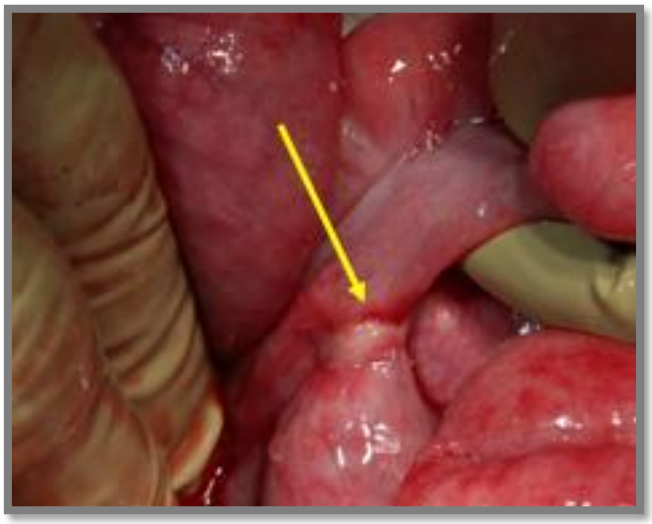

Figure 7

The anastomosis had well healed and was almost unrecognizable with a complete smooth surface and soft on palpation. The only serosa disruption was at the side of the PDS stitch (yellow arrow), see *Figures 8, 9* below.

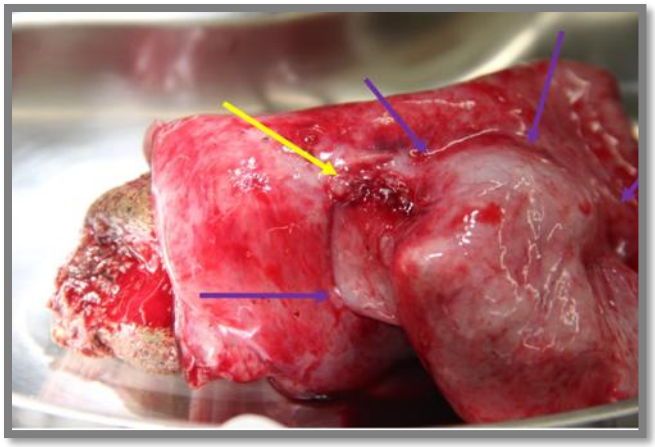

Figure 8

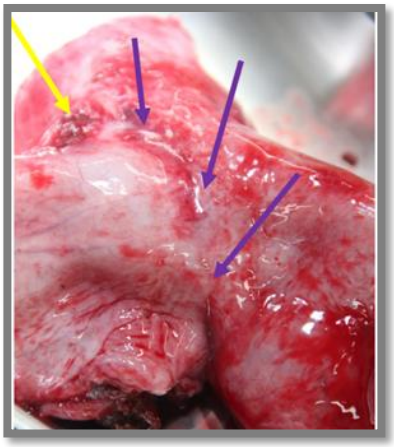

Figure 9

After dissecting the anastomosis, macroscopic inspection revealed a complete smooth surface and supple anastomosis. The inner concentric staple line had disappeared completely and the outer transverse staples were covered with serosa and no adhesions had formed (see *Figures 10, 11, 12*).

Figure 10

Figure 11

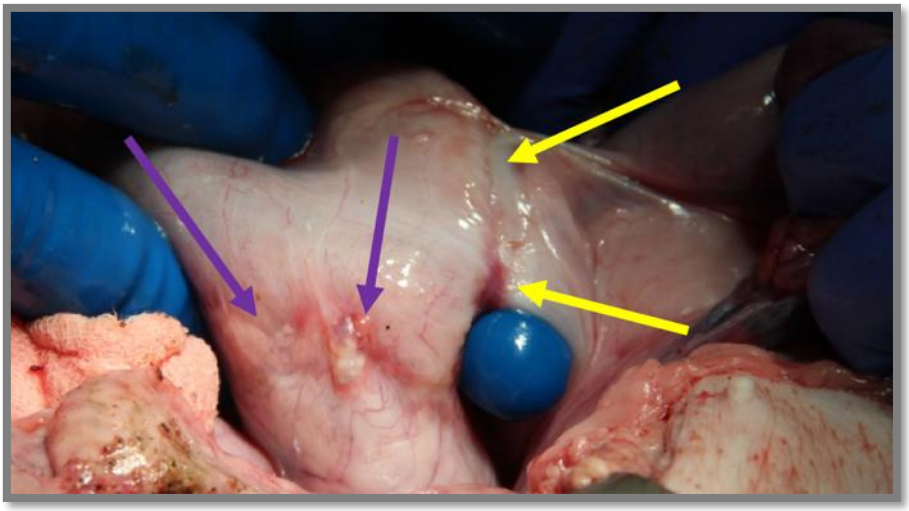

Figure 12 Yellow arrows show the adhesion of the GIA staple line with the abdominal wall. The TOP staple line is at the purple arrows.

The second pig (no. 6) was operated on in the same way. Surgery and postoperative course were uneventful. After 7 days, the pig was sacrificed. There were more adhesions on opening the abdominal wall through the scar than found in pig 5. Intra-abdominally there were no adhesions except for again a GIA staple line that was firmly adhered to the abdominal wall. No adhesions were found near the anastomotic site. The anastomosis felt smoothly and soft. After dissection, it was clear that the anastomosis had healed in a similar manner as in pig 5. The surface was smooth and the anastomotic line was hardly visible. The serosa had covered the transverse staples completely (see *Figure 13*).

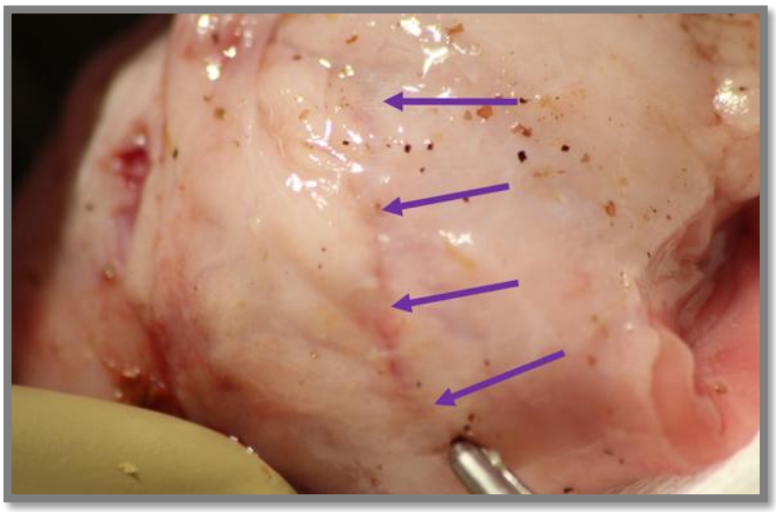

Figure 13 .

Only one concentric staple was identified and the rest had disappeared and one transverse staple was seen at the inner site of the anastomosis (*Figures 14*, *15*).

Figure 14

Figure 15

The serosal coverage of the outer transverse staples was complete and very smooth in both anastomoses. The inner concentric staple line had disappeared. The anastomoses were supple and could easily be stretched radially. Since the inner concentric staple line had disappeared, only radially placed staples were in place in a well healed, non-fibrotic anastomotic healing area. The configuration of the radial staples and the absence of stricturing fibrosis made the radial distension possible. Clinically this might lead to a diminished rate of anastomotic strictures.

In summary: Our porcine experiment with a follow-up of 7 days showed that the anastomoses in both pigs using the experimental TOP stapler had healed well.

Third experiment: comparing short time healing of conventional stapler and TOP stapler healing

The TOP stapled anastomosis healed very well in 7 days in our second experiment. The third experiment was set up to compare healing between the conventional circular stapler and the experimental stapler. A short follow-up of 3 days was chosen, in order to investigate eventual differences in the early phases of wound healing. In two pigs two anastomoses were planned: one with the TOP stapler and one with the conventional stapler. The anastomoses were evaluated both macroscopically and microscopically.

In April 2017, the first pig of this study (no. 7, weight 79 kg) was operated. In the sigmoid colon two anastomoses were performed: one with a standard conventional stapler 28 mm and one with a TOP experimental stapler. At autopsy after 3 days, both anastomoses were intact and showed uneventful healing. The only difference was that there was a blood clot on the conventional anastomosis (*Figure 16*).

The outer transverse staples of the TOP stapler were visible on the serosal side and not yet covered by serosa, nor adhesions (*Figure 17*). Although apposition seems loose, our first experiment showed that this loose apposition resulted in uneventful healing without leakage after 7 days.

Figure 16

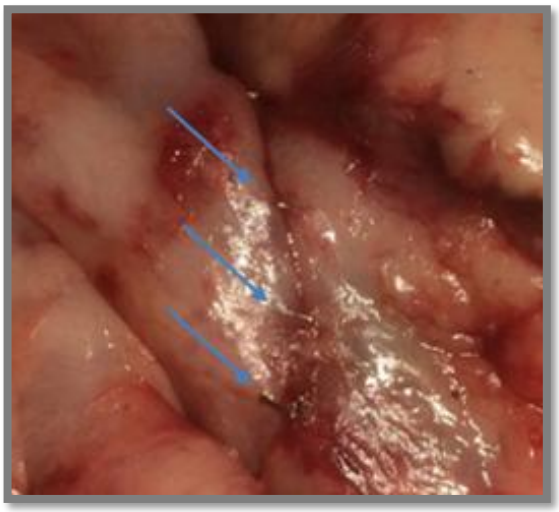

Figure 17

At the inner concentric staple line of both the anastomoses circular necrosis was evident on the mucosa (like we saw in our first experiments) (*Figure 18*). The conventional anastomosis was covered with some adhesions on the serosal side and had healed properly.

Figure 18

In pig 8 (weight 73 kg) similar results were obtained. shown with some fibrin deposition.

Histology specimens were prepared, after removing staples. One-sided bowel ends were sliced and studied. Beside a smaller necrotic area in the TOP stapler bowel end, no differences were found.

Conclusion

The new TOP stapler is capable of anastomosing intestinal colon segments of pigs in a way that leads to proper and uneventful healing both after 3 and 7 days. The macroscopic appearance of the anastomosis is satisfactory, the fusion of the serosal layers after 7 days appears complete and provides a complete coverage of the outer transverse staples. The conceptual purpose of the outer staples therefore has been achieved. The inner concentric staple line had disappeared completely after 7 days enabling a supple stretchable anastomosis, as hypothesized. In our experiment with 3-day follow-up, we showed that the TOP stapler achieved similar wound healing as compared to the conventional stapler. It was found that the only adhesions in the experiments were found at the serosal site of the anastomoses that were performed with the conventional staplers and at the GIA staple lines. There were no adhesions formed in reaction to the anastomoses with the TOP staplers.

These experiments have shown that the TOP stapler functions well in pigs and is at least non-inferior to the conventional stapler. Results like the supple stretchable texture of the anastomosis and the absence of leakage and adhesions indicate that the TOP stapler creates better healing conditions than the conventional stapler.

See also the following documents:

- *Optimizing stapled gastro-intestinal anastomosis*

References

1. Wenger FA, Szucsik E, Hoinoiu BF, Ionac M, Walz MK, Schmid KW, Reis H. A new anastomotic leakage model in circular double stapled colorectal anastomosis after low anterior rectum resection in pigs. J Invest Surg, 2013: 26; 364-72.