Optimization and assessment of a novel gastric electrode anchoring system designed to be implanted by minimally invasive surgery

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ABSTRACT

A novel electrode anchoring design and its implantation procedure, aiming for a minimally invasive solution for gastric electrical stimulation, are presented. The system comprises an anchor made of a flexible body embedding two needle-shaped electrodes. The electrodes can easily switch from a parallel position – to pierce the stomach – to a diverging position – enabling them to remain firmly anchored into the muscular layer of the stomach. Key device parameters governing anchoring stability were assessed on a traction test bench, and optimal values were derived. The device was then implanted in six dogs by open surgery to assess its anchoring durability *in vivo*. Computed tomography images showed that the electrodes remained well placed within the dogs' gastric wall over the entire assessment period (more than one year). Finally, a prototype of a surgical tool for the minimally invasive device placement was manufactured, and the anchoring procedure was tested on a dog cadaver, providing the proof of concept of the minimally invasive implantation procedure. The use of our electrode anchoring system in long-term gastric electrical stimulation is promising in terms of implantation stability (the anchor withstands a force up to 0.81 N), durability (the anchor remains onto the stomach over one year) and minimal invasiveness of the procedure (the diameter of the percutaneous access is smaller than 12 mm). Moreover, the proposed design could have clinical applications in other hollow organs, such as the urinary bladder.

Key Words: Electrode anchoring ; Percutaneous implantation ; Single incision surgery ; *In-vivo* validation ; Gastric electrical stimulation

INTRODUCTION

Obesity has reached pandemic proportions in the 21st century. According to the World Health Organization, more than 1.9 billion adults are overweight and over 650 million adults are obese worldwide. The related costs for the medical care system were estimated to be about $150 billion per year in the U.S., and they increase every year [1–3].

While bariatric surgery remains the most common solution to treat obese patients having failed to respond to dietary and behavioral therapies, there are concerns regarding procedure-related complications and mortality [4,5]. Adaptations that reduce the invasiveness of the surgery and avoid permanent changes in the gastrointestinal tracts have been proposed [6]. As an alternative, gastric electrical stimulation (GES) has shown promising results, reducing weight and food intake in humans and animal models [7–12]. However, current gastrostimulators are bulky and they are usually implanted by multi-incision laparoscopy, which remains a relatively expensive and invasive procedure [13].

Although laparoscopy is the most common method to place gastric stimulation electrodes [14–19], some researchers explored the advantages of single incision alternatives such as percutaneous implantation of temporary GES electrodes [20,21]. They used homemade temporary leads to access the muscular layer of the stomach without piercing the gastric mucosa. The electrodes were kept implanted for a mean time of 26 days, in 27 patients with drug-refractory nausea and/or vomiting. Another team [22] studied both percutaneous and endoscopically placed temporary electrode anchoring on the stomach of 20 patients. These studies were conducted to select patients that would benefit from a permanently implanted stimulator [18]. They have demonstrated the feasibility of temporary minimally invasive percutaneous electrode placement for GES, but did not address the prerequisites for long-term, minimally invasive anchoring systems for GES therapy.

Besides laparoscopic and single incision percutaneous implantation, entirely endoscopic procedures have been studied to anchor a GES device in the inner wall of the stomach without surgery [23]. However, rare practical applications have been reported, and the technique has remained limited in anchoring durability and functionality [13,24].

This article presents a novel electrode anchoring design, providing a less invasive and long-term implantation solution relying on a single incision percutaneous access with a single step release design for safe and fast anchoring of GES electrodes in the muscular layer of the stomach. Functional study, validation of the anchoring durability *in vivo* and proof of concept of the surgical procedure are provided. The presented design is protected by a patent published in June 2020 (WO 2020/126770).

METHODS

Electrode design and implantation procedure

We aim to position and secure a two-electrode anchor onto the gastric wall, through a single incision percutaneous access. A single step release reduces the complexity and the duration of the surgery. The small diameter of the access (<12 mm) enables the percutaneous incision to be dilated rather than cut, hence reducing the resulting scar.

The proposed anchor design and dimensions are presented in Figure 1. The anchor is made of a flexible silicone substrate embedding two stainless steel electrodes that diverge from the center plane in unconstrained situation (Figure 1a). The silicone body shape is characterized by an upper ellipse (with principal axes of 5 mm and 10 mm) and a lower ellipse (with principal axes of 14 mm and 6 mm), on a height of 7 mm. The electrodes come out of the lower part of the silicone body with a variable angle α that defines their deviation with respect to the vertical axis. When a force is applied on both sides (e.g. by a dedicated implantation tool), the device is bent until the electrodes are parallel, to ease the piercing of the gastric wall (Figure 1b). The needle length is designed to pierce the muscular layer of the gastric wall without penetrating the mucosal layer, to prevent leakage of the luminal content. Once the electrodes are inserted into the gastric wall over their entire length, the tool releases the anchor. The silicone acts like a spring so that the anchor recovers its initial shape (Figure 1c), preventing it from being dislodged.

The proposed implantation method is based on the laparoscopic-assisted percutaneous endoscopic gastrostomy [25]. This procedure enables the access to the interior of the stomach with a single dilated hole, using T-fasteners to fix the gastric wall on the internal abdominal wall. It has been proven a safe and minimally invasive procedure. Because we do not aim to access the interior of the stomach, we do not pierce the gastric wall with the dilation needle in our procedure.

Our implantation method, detailed in Figure 2, consists in inserting a trocar (outer diameter of 12 mm) with a dilating distal end to penetrate the skin and the abdominal wall, and access the outer surface of the stomach, then positioning and inserting the anchor into the gastric wall using a dedicated tool.

Under gastroscopic visualization, an artificial pocket between the parietal and the gastric serosae is delimited by four T-fasteners in a square with 2 cm sides (Figure 2a) to host the anchor. It fixes the position of the pyloric antrum on the parietal wall. The fasteners are slightly tightened at this stage. A hollow needle is inserted through the skin and the abdominal wall at the center of the delimited area, and a guide wire is inserted until it is observed to push the gastric wall towards the lumen within the middle of the square formed by the toggles of the T-fasteners. The access is then smoothly widened with a dilation balloon until a 12 mm outer diameter trocar can be placed with a dilation distal end (Figure 2b). The trocar enables the insertion of the dedicated tool to access the stomach (Figure 2c). The tool is made of a hollow cylinder with, at its distal end, a cavity shaped to hold the anchor in its compressed configuration (i.e. parallel electrodes). An inner cylinder is inserted, from the proximal end, to push the electrodes towards the stomach until they pierce the gastric wall (Figure 2d). The insertion tube is removed and, once outside the tool, the anchor expands in its deployed configuration with the electrodes in the muscular layer of the stomach (Figure 2e). The T-fasteners are then tightened to their full extent to isolate the anchor in the pocket (Figure 2f). Over time, fusion of the serous tissues will permanently seal the pocket edges [26], further improving the anchoring durability. A prototype of the tool is presented in Figure 3.

Validation of the design

The validation of the design has been carried out in three separate studies. First, a test-bench characterization was conducted to measure the anchoring stability, i.e. the force required to dislodge the anchor from the gastric wall. Then, six anchors were implanted by open surgery in six dogs for *in-vivo* assessment of the long-term anchoring durability. Open surgery was used to avoid the

uncertainties of the newly developed single hole surgery at that stage of the study, hence focusing on anchoring durability only. Finally, the minimally invasive implantation procedure was validated on a dog cadaver.

Analysis of parameters governing anchoring stability

The bending stiffness of the silicone body (i.e. its resistance against bending deformation) and the angle between the electrodes (α in Figure 1) were investigated. These two parameters directly influence the stability of the anchoring. The force needed to remove the anchor from the gastric wall was evaluated for various values of bending stiffness and angle α.

The angle α could physically range from 0° to 60°, as an angle larger than 60° would make the implantation highly impractical. The 100%-modulus of the silicone (i.e. the tensile force to apply on a sample section, in Pascal, to reach 100% of deformation) was used to assess the bending stiffness. It is a common indicator that can be obtained from some silicone rubber manufacturers or through straightforward traction tests. Having fixed the anchor geometry, the 100%-modulus was the best candidate to evaluate the bending stiffness in this experiment, because the bending stiffness only depends on the body geometry and the modulus of the material. The 100%-modulus of our samples could be varied from 140 to 600 kPa, which was considered a reasonable range for ergonomics and ability to be bent when used with typical devices (based on a preliminary study). The different moduli required for the experiment were obtained by combining different silicone rubbers (MED4-4220, MED6019 from Nusil[TM] and EcoFlex 00-30 from Smooth-On).

A factorial design was used to evaluate the impact of these two parameters on the dislodgement force (using *Design Expert 9*) [27]. This commonly used first approach was proven sufficient by the data presented in the result section. However, with a view to extend the analysis to a composite centered design if significant lack of fit would be observed, we must consider taking a margin in the studied range of parameters. Consequently, based on the achievable range of 0° to 60° for the angle

and 140 to 600 kPa for the 100%-modulus, the actual studied range was reduced to 8°–51° and 217–533 kPa for the factorial design.

Anchors were manufactured and assessed on a traction bench to retrieve the dislodgement force (see Figure 4), and the test sequence was randomized, in order to avoid any influence from external, non-controlled, parameters on the result. A portion of a pig stomach (65 mm * 35 mm) was cut and placed into a clamp designed to hold it. For each sample, the anchor was manually bent to hold the electrodes parallel, then inserted inside the gastric wall and released. A rigid handle was fixed on the upper side of each anchor. To measure the force needed to extract an anchor from the gastric wall, a Lloyd LS1 traction bench (Universal Test Machine, AMETEK, USA), with a YLC-0010-A1 load cell (0 to 10 N, 0.5% accuracy, 10^{-4} N resolution) was used in quasi-static traction (5 mm/min motion speed).

In-vivo assessment of the anchoring durability

A batch of anchors with optimal parameters (as defined by the methodology presented in the previous section) was manufactured. An anchor was implanted in six male dogs, through open surgery by midline celiotomy, to assess the long-term anchoring capability of our design. The experimental protocol was approved by the Animal Care and Use Committee of the University of Liège (ethical protocol 16-1818). After a 24-hour fast, the dogs were premedicated with methadone, induced by propofol IV and maintained under general anesthesia with isoflurane throughout the surgery, with continuous monitoring of anesthetic parameters. The anchors were placed immediately caudal to the ventral aspect of the lesser curvature of the stomach, and parallel to it, a location proven efficient for gastric electrical stimulation [9]. With a view to mimic the future minimally invasive procedure, a gastropexy was performed to embed the anchor in a pocket delimited by the abdominal wall and gastric serosa. The resulting pocket was therefore similar to the one created by the T-fasteners tightening in the minimally invasive procedure.

All dogs were checked on a daily basis during at least twelve months following implantation, and any clinical abnormality (e.g. pocket inflammation, vomiting, barking, diarrhea, sialorrhea) was recorded.

The position of the electrodes was evaluated on repeated CT-scan (Siemens, SOMATOM Sensation 16, Erlangen, Germany; Acquisition parameters: tube voltage 120 kV, reference tube current 88 mA, and pitch 0.7 – 1.15 mm). The scan tube current was modulated by automatic exposure control (Care Dose, Siemens Medical Solutions, International). The image data set were reconstructed using parameters of 300 mm of field of view, 512 x 512 matrix, 1.5 mm slice thickness and B-30f reconstruction algorithm. For practical reasons, the six dogs were not implanted on the same day, but the scanning sessions were performed on the same day, resulting in different time intervals between implantation and imaging for the individual dogs. The first scans were performed one to five months after placement of the implant and the second ones ten to fourteen months after the implantation. The images served to assess whether the electrodes were correctly placed inside the gastric muscular layer without penetration into the gastric lumen. A contrast medium (Ultravist® 300, Bayer, 2 ml/kg) was injected intravenously before image acquisition, to highlight the mucosa which appears hyperattenuating (i.e. brighter) than the remaining parts of the gastric wall, thanks to its higher vascularization and secondary contrast enhancement. Images were reviewed by one reader specialized in veterinary CT images reading (GB).

Assessment of the minimally invasive implantation procedure

The manufactured prototype was used to validate the implantation procedure detailed in Figure 2 in a dog cadaver, using commercially available Entuit™ Secure T-fasteners (GIAS-SRM-ADJ-3, Cook Medical Inc.). The gastroscopic visualization was performed with a GIF-160 gastroscope connected to a CLV-160 light source and CV-160 video processor (Olympus Corporation). After completing the procedure, an abdominal approach was carried out to evaluate the quality of the implantation. The anchoring area was dissected to analyze the pocket obtained by use of the T-fasteners as well as the anchor placement within the gastric wall.

RESULTS

Analysis of parameters governing anchoring stability

Based on the factorial design made of 15 runs given in Table 1, the ANOVA analysis (Table 2) shows the force to be linearly proportional to the angle α between the electrodes (with no effect of the modulus), according to the relationship shown in Figure 5. The tensile force needed to dislodge the anchor was 1.12 ± 0.04 N when angle α was maximum (60°). The angle α had a significant effect on the dislodgement force of our anchors, but the flexibility did not. Therefore, any silicone could be used (within the studied range).

While the angle α should be maximized, the ease of implantation is another important constraint for future uses. An angle of 45°, corresponding to a dislodgment force of 0.81 N, was chosen as a good compromise between anchoring quality and ergonomics. The MED4-4220 was chosen because of its 100%-modulus in the middle of the tested range, and its advantageous properties (such as biocompatibility) in a biomedical setting [28].

In-vivo assessment of the anchoring durability

All surgeries were performed without any complication and the dogs recovered well from the procedure and anesthesia. No abnormal symptoms were noted throughout the duration of the experiment (over one year), suggesting that the electrodes had not pierced the mucosa. This was further verified by expert analysis of the CT scan images (GB), which confirmed that the electrodes were indeed located in the muscular layer without piercing the gastric mucosa in all six dogs. Figure 6 shows representative CT scan images with one of the two electrodes that are located in the remaining part of the gastric wall, without piercing the mucosal layer.

Assessment of the minimally invasive implantation procedure

The minimally invasive implantation procedure was successfully carried out on a dog cadaver. Illustrations of the key steps are presented on Figure 7 and in Video 1. While placing the T-fastener needles (Figure 7a, corresponding to Figure 2a), the simultaneous gastroscopy enabled the surgeon to have a feedback on the exact positioning of the four T-fasteners, whose alignment was considered as a key point for the subsequent successful placement of the anchor. Indeed, placing them parallel was paramount to obtain a proper delimitation of the pocket surrounding the anchor device. Figure 7b (corresponding to Figure 2d) shows, from outside and inside the stomach, the implantation tool that pushes the anchor so that the electrodes pierce the gastric wall (without reaching the lumen). Again, the gastroscopy images allowed the surgeon to follow the electrode insertion from the lumen. Placement of the anchor without piercing the mucosa was performed easily. Figure 7c (corresponding to Figure 2f) shows the implantation area after tightening of the T-fasteners. The cable linked to the anchor is accessible for a future connection to a dedicated gastric stimulator.

The area of interest was dissected to confirm the proper creation of the gastropexy pocket, and the correct positioning of the anchor. The pocket was successfully created and it enclosed the anchor as desired. Subsequently, two out of the four fasteners were removed to obtain a view of the implanted anchor to confirm proper positioning of both electrodes in the gastric wall (Figure 7d), and the stomach was opened to obtain the corresponding inner view (Figure 7e). Both electrodes were positioned in the muscular layer as desired, without having pierced through the mucosal layer. The minimally invasive anchor placement procedure was therefore proven feasible.

DISCUSSION

This paper presents a novel system for minimally invasive placement and long-term anchoring of electrodes into the gastric wall. First, we have shown the importance of the angle α between the electrodes to increase the stability of the anchor, while there was no influence of the silicone flexibility. There is a compromise between a stronger anchor fixation (i.e. larger values of α) and better implantation ergonomics (i.e. smaller values of α). We believe an angle of around 45° would be optimal. The silicone flexibility was proven to have no effect on the dislodgment force within a large range and can thus be fine-tuned based on implantation ergonomics. Second, this optimized anchoring design was proven to remain in its implanted position in the gastric wall for more than one year, in six dogs, in an *in-vivo* experiment. No medical issues nor signs of discomfort were observed during the entire length of the experiment. Finally, a prototype of the implantation tool was designed and successfully used on a dog cadaver to provide a proof of concept of the feasibility of the minimally invasive procedure to implant the anchors.

When studied on a traction test bench, no correlation was found between the silicone flexibility and the dislodgement force of the anchor. This was expected considering the flexibility of the silicone compared to the one of the gastric wall. When the anchor is pulled, a force is applied on both the anchor and the stomach. With a modulus of around 1.9 kPa [29], the gastric wall is much more flexible (by two orders of magnitude) than the silicones we tested. The stomach is therefore bent under the constraints from the needles, while the anchor barely deforms.

Our implantation procedure aims to propose an efficient and less invasive alternative to laparoscopy for GES therapy. While a minimally invasive approach for percutaneous electrode positioning has been demonstrated to screen patient response to GES [21,30], it was only meant for temporary use (and assessed this way). Our solution uses an implantation procedure that is minimally invasive

(leaving only one small scar for the patient) and quick (hence also reducing its cost) to deliver an anchor that remains securely fixed into the gastric wall for an extended period of time.

Our anchor is meant to remain in the patient for decades without migration. Its anchoring durability was assessed in vivo for one year to ensure the device remains properly positioned even when affected by the various motions and vibrations of daily life. Moreover, the anchor device weighs 0.9 ± 0.05 g (measured with a Kern PCB 2005-2), leading to a gravitational force of about 8.8 mN, which was proven insufficient to dislodge the anchors in our experiment. In dogs, this force is applied in the longitudinal axis of the anchor, working as a pulling force, in a comparable situation to the traction bench test assessing the anchoring stability. In humans, the gravitational force is expected to act transversally on the anchor body. In both cases, the force is two orders of magnitude lower than the estimated 0.81 N required to dislodge the anchor (when α equals 45°). In this regard, we believe that the lightness of the device makes the gravitational force acting on it negligible.

While our *in-vivo* experiment only assessed anchoring durability over one year, it is reasonable to assume that the chances of migration after that period of time are small. Body reactions such as adhesion between peritonea or fibrosis are working against migration. In this regard, it can be assumed that the one-year experimentation covers the most critical period in terms of migration.

Biocompatible materials were used to manufacture the anchors that were implanted in the dogs for anchor durability assessment. The anchor body was made of MED4-4220 (medical grade) silicone and the needles were made of stainless steel. Since dogs were not sacrificed at the end of the study, no toxicity tests were performed. However, the regular clinical observations confirmed the absence of symptoms that would be related to material toxicity.

The assessment of the minimally invasive implantation procedure on a dog cadaver confirmed the feasibility of anchoring the electrodes through a single dilated percutaneous access of 12 mm. The key role of the simultaneous gastroscopy was highlighted, both to position the T-fasteners and to confirm the anchor placement. Based on this preliminary trial and after video analysis, the surgeons

(HdR, EB) have estimated that the total duration of the procedure will not exceed 15 minutes (excluding optional stimulator placement and test).

Our anchoring system was initially designed to perform gastric electrical stimulation as a treatment against obesity. It may give an interesting less-invasive alternative to bariatric surgery, that is linked to procedure-related complications and mortality [4,31]. However, even if gastric electrical stimulation has shown promising results in reducing weight and food intake [7–12], bariatric surgery still outperforms it. Improving the efficiency of gastric electrical stimulation would reduce this gap. In this regard, our team has developed a gastric stimulator that delivers individualized stimulation parameters and that adapts them over time to counter habituation, showing promising results on dogs' food intake and weight loss (unpublished results). It could offer an attractive solution from both weight loss and patient acceptance perspectives.

While our anchor is designed to be inserted in the gastric muscle, its use can be extended to other hollow organs to which a long-term access is required. Urinary bladder monitoring and stimulation, for example, is another application of interest. Incontinence is still an unsolved issue for about 200 million people worldwide despite several advances in the available treatments [33]. Spinal cord injured patients, in particular, suffer from neurogenic bladder. Managing bladder functions in these patients is a patient and research priority [34–38]. Health issues and incontinence could be avoided if sensory information, such as bladder fullness, was available. Proposing a device able to sense a bladder event and alert that bladder emptying is required would be an important advancement. Besides, neuromodulation has had a positive impact on the treatment of the bladder for patients with neurologic conditions [33,39]. Previous studies [33] have shown that conditional stimulation, i.e. stimulating only when required in a closed loop feedback, would allow more effective bladder management. Here again, the missing piece of the puzzle, for effective conditional stimulation, would be a reliable method for sensing bladder activity. Monitoring bladder contractions and/or bladder pressure is, however, a challenging task. Research in this area is mainly focused on nerve

monitoring. However, low signal to noise ratios make it difficult to distinguish bladder pressure and contraction information from other information carried in the nerve [33]. Having the possibility to place an anchor on the urinary bladder wall for both recording and stimulation can be an asset: we have a direct access to physiological measures, including bladder strain, pressure and muscle activity, that could more directly and specifically reflect the bladder activity.

Beside monitoring and stimulation of hollow organs, many other applications of the described anchoring system are foreseen. For instance, the flexible body of the anchor could embed a hollow channel to ensure the delivery of specific chemicals in a targeted area to achieve chronic drug therapies. Also, the metallic pins could be rearranged to offer an advantageous stapling system having the silicone body obtruding a targeted fistula to be closed. Altogether, we hope this anchoring system will pave the way for various minimally invasive applications.

CONFLICT OF INTEREST AND ETHICS

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SUPPLEMENTARY MATERIAL

A video summarizing the minimally invasive implantation procedure carried out on a dog cadaver is

provided in Video 1 (http://gofile.me/3bw84/JxRrI082U).

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TABLES

Run	Angle [°]	100%-Modulus [kPa]	Dislodgement force [N]
1	30	355	0.47
2	30	355	0.46
3	30	355	0.53
4	30	355	0.38
5	51	217	1.05
6	51	217	0.70
7	51	533	0.89
8	51	533	0.77
9	9	217	0.05
10	9	217	0.10
11	30	355	0.48
12	30	355	0.54
13	9	533	0.06
14	9	533	0.07
15	30	355	0.44

Table 1: Experimental runs used in the factorial design with the corresponding dislodgement force measured with the traction bench.

Source	Sum of Squares	Degrees of freedom	Mean Square	F-value	p-value
Model	1.23	3	0.409	51.29	< 0.001*
A - Angle	1.23	1	1.23	153.66	< 0.001*
B - Modulus	0.0016	1	0.0016	0.2047	0.6598
AB	0.0006	1	0.0006	0.0768	0.7868
Residual	0.0877	11	0.008		
Lack of Fit	0.0003	1	0.0003	0.0306	0.8646
Pure Error	0.0874	10	0.0087		
Cor Total	1.31	14			

*Table 2: ANOVA analysis derived from the factorial design, angle is shown to be the only significant design parameter. * indicates significance.*
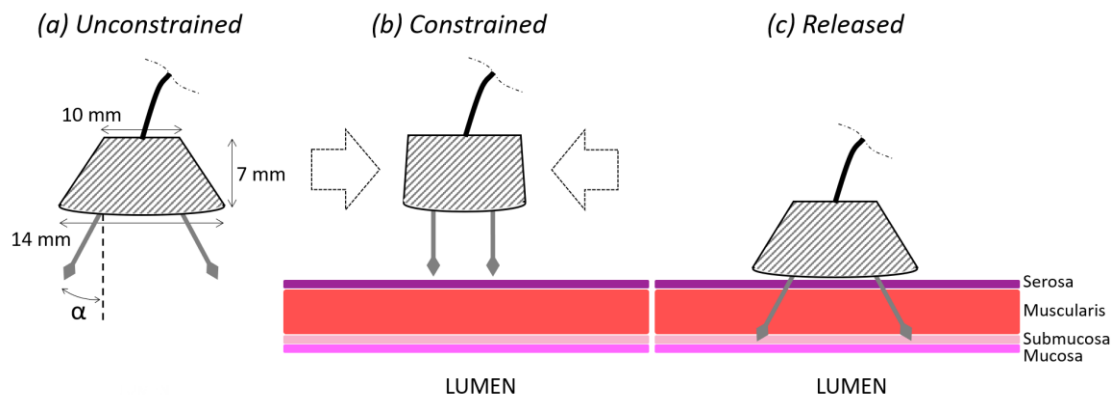
FIGURES

Figure 1: (a) Unconstrained anchor with dimensions, and α the deviation angle of the electrode. (b) Anchor bent by lateral forces. (c) Anchor released within the gastric wall.
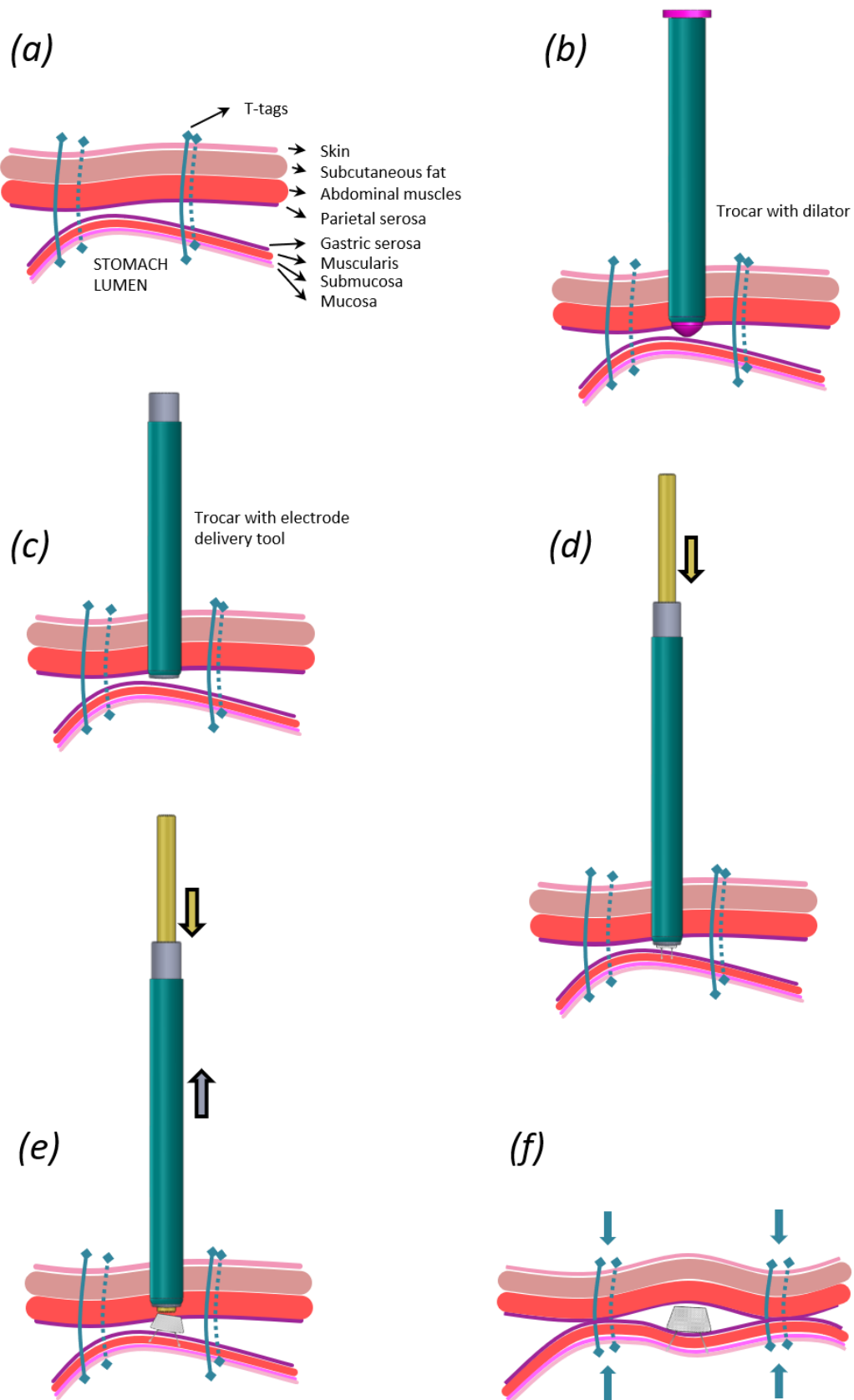
(a)

(b)

T-tags

Skin
Subcutaneous fat
Abdominal muscles
Parietal serosa
Gastric serosa
Muscularis
Submucosa
Mucosa

STOMACH
LUMEN

Trocar with dilator

Trocar with electrode
delivery tool

(c)

(d)

(e)

(f)

Figure 2: Percutaneous procedure to place the anchor in the gastric wall. Top: parietal wall; bottom: pyloric antrum (a) Positioning of the T-fasteners. (b) Trocar insertion by dilation. (c) Placement of the tool delivering the anchor. (d) Insertion of the electrodes into the muscle layer. (e) Release of the anchor. (f) Tightening of the fasteners.

Figure 3: Prototype of the implantation tool made of a trocar with dilation tip (lower part), and the electrode delivery tool (upper part).
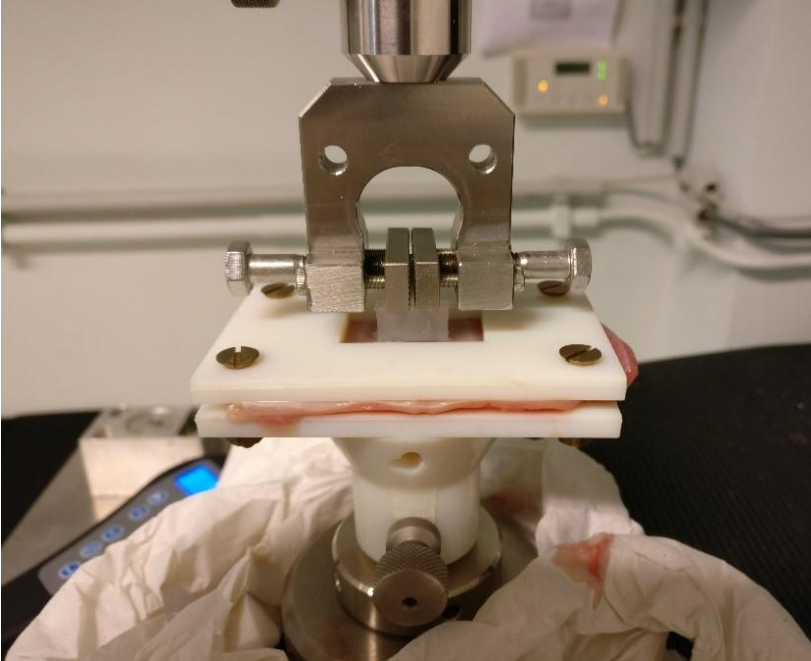

Figure 4: Traction test bench setup with the lower part holding the gastric wall sample and the upper part pulling on a handle fixed on the anchor.
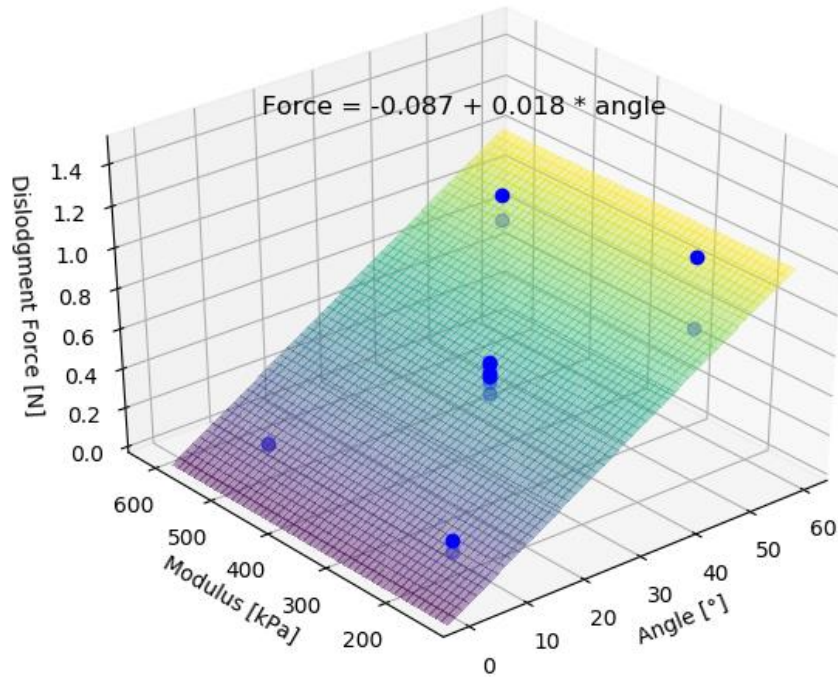
Figure 5: Dislodgment force with respect to the electrode angle α and the silicone 100%-modulus. The dots represent the experimental points and the surface the linear model derived from the factorial design.
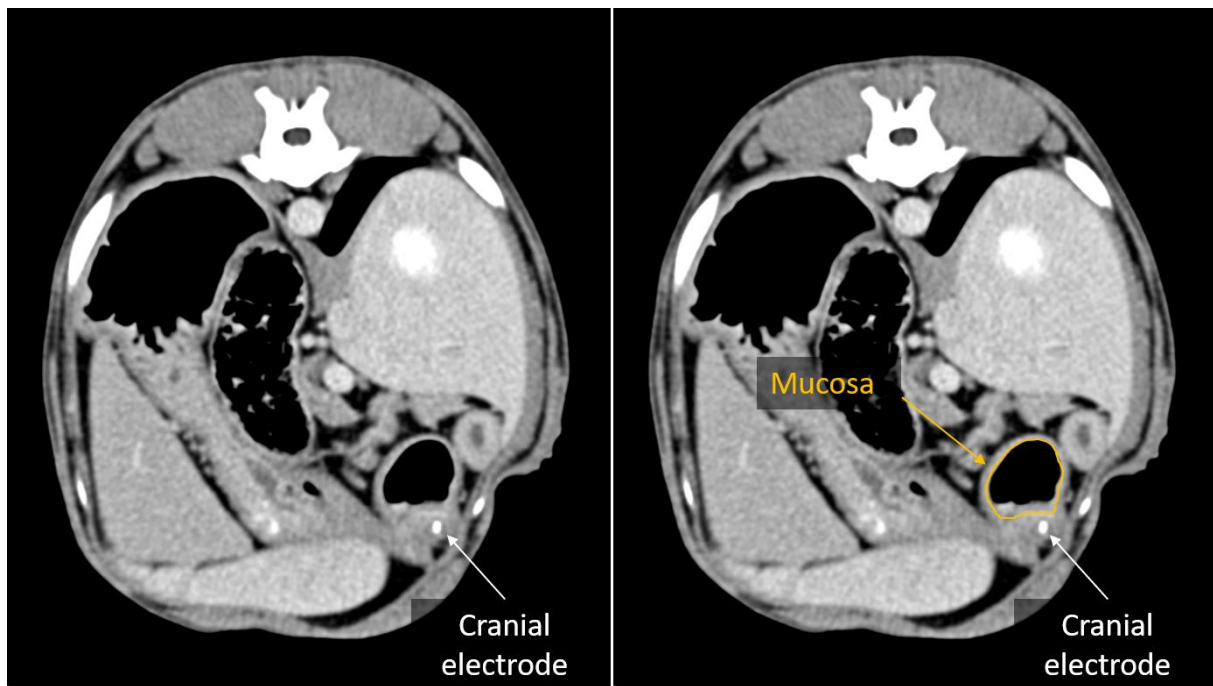

Figure 6: CT scan image (soft tissue window, after contrast medium administration), acquired at the electrode level, near the dog pylorus, without (left) and with (right) tracing out the mucosal layer which appears hyperattenuating (brighter) than the remaining part of the gastric wall due to contrast enhancement (ten months after implantation).
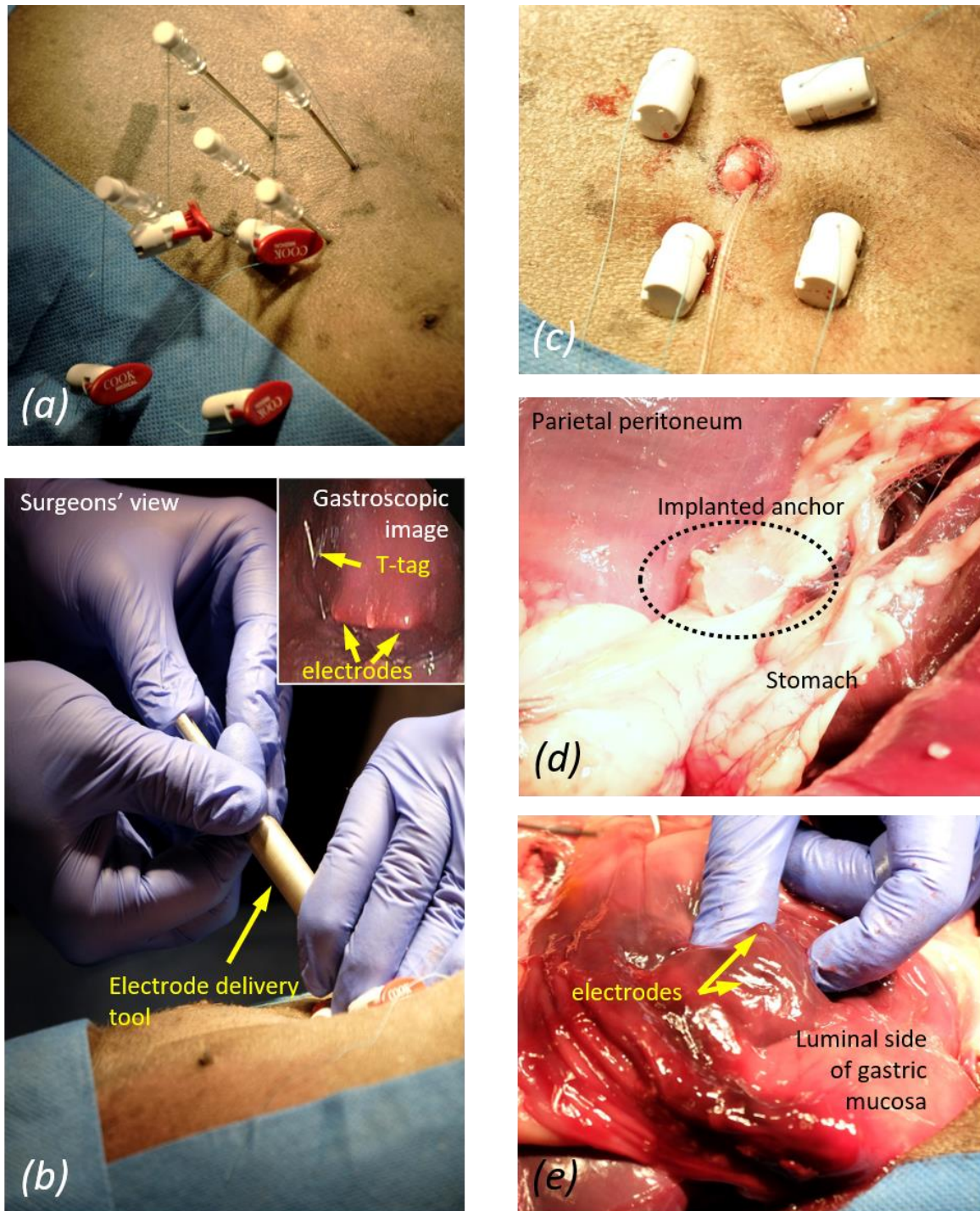
Figure 7: Percutaneous implantation procedure performed on a dog cadaver. (a) Positioning of the T-fasteners. (b) Insertion of the electrodes viewed from the outside and from the lumen. (c) T-fasteners tightened. (d) Anchor in the gastric wall after dissection. (e) Lumen view of the electrode location after dissection. The mucosa is slightly elevated by the tips of the electrodes, which did not pierce this layer.