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Over-the-Scope-Clips Can Be Fired Safely Over a Guidewire: Proof of Concept in an Ex-Vivo Porcine Model

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ABSTRACT

Background and Objectives: To assist in achieving optimal position when deploying over-the-scope (OTS)-clips, the concept of cannulating the defect with a guidewire, backloading the endoscope onto the wire, and firing the OTS-clip over the wire with subsequent wire removal has been demonstrated. The safety of this technique has not been evaluated.

Methods: An ex-vivo porcine foregut model was utilized. Biopsy punches were used to create 3-mm diameter full-thickness gastrointestinal tract defects through which a guidewire was threaded. An endoscope was backloaded over the wire and OTS-clips (OVESCO, Tuebingen, Germany) were fired over the mucosal defect and wire. The wire was removed through the endoscope and the removal difficulty was graded using a Likert scale. This process was repeated for each unique combination of nine OTS-clip types, two wire types, four wire angles, and three tissue types. Statistical analysis included *t* test and ANOVA.

Results: Two hundred sixteen OTS-clip firings with wire removal attempts were performed with the following Likert score breakdown: 1 – No difficulty (80.6%), 2 – mild difficulty (16.2%), 3 – moderate difficulty (2.3%), 4 – extreme difficulty (0.9%), and 5 – unable to remove (0%). Statistically significant differences were noted in removal difficulty between OTS-clip sizes ($p < 0.05$). No differences were identified between clip teeth types, wire types, tissue types, and wire angles ($p > 0.05$).

Conclusion: In this ex-vivo model, the guidewire was successfully removed through the endoscope in all cases. This technique can be employed to facilitate OTS-clip closure of gastrointestinal tract defects, but further study is indicated before wide clinical implementation.

Key Words: Endoscopy, Fistula, Guidewire, Over-the-scope clip.

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INTRODUCTION

The management of gastrointestinal (GI) tract defects continues to evolve as novel endoscopic devices and techniques are demonstrated. First introduced in 2007, over-the-scope (OTS)-clip systems have been utilized in a wide range of clinical scenarios and novel applications of this device continue to broaden its clinical utility.[1] Originally approved for the management of GI bleeding, OTS-clips have subsequently been utilized for the closure of acute, iatrogenic GI tract defects, including full-thickness perforations.[2] More recently, OTS-clips have been used in the successful closure of nonacute, full-thickness GI tract defects including both leaks and fistulae.[3] These minimally invasive endoscopic techniques spare patients the morbidity of more invasive surgical techniques.

For patients with fistulae involving their GI tract, management often involves a prolonged period of nonoperative management complicated by continued fistula output which is eventually followed by complex operative repair.[4] The morbidity and mortality in these patients approaches 50% and 10% respectively, and increases with medical comorbidity and surgical complexity.[5,6] OTS-clip management offers an attractive therapeutic alternative with the ability to both quickly alleviate symptoms related to fistula output and avoid the need for further surgical intervention. Numerous studies have demonstrated successful

OTS-clip management of a wide variety of GI tract fistulae including tracheoesophageal, enterocutaneous, gastrocolic, colovaginal, and colovesical fistulae.[7–10]

Despite these documented successes of fistula closure with OTS-clips, recent clinical experience has demonstrated notable drawbacks which limit its applicability.[9] First, accurate endoscopic fistula identification can be difficult to achieve in heavily diseased bowel (e.g. diverticular disease) and precise maneuvering of the OTS-clip into the correct position is, at times, impossible. Secondly, OTS-clips perform best when fired in an "end-on" position, meaning the scope, clip, and tissue are aligned along one axis; however, this position can be difficult to achieve depending on fistula location. Therefore, the concept of cannulating the defect with a guidewire, backloading the endoscope onto the wire, and firing the clip over the wire with subsequent wire removal through the endoscope has been demonstrated.[9] However, the safety of this technique, particularly related to the theoretical concern for wire entrapment by the clip, has not been previously evaluated. The goal of this study was to evaluate the safety of firing an OTS-clip over a wire in an ex-vivo porcine model with the hypothesis that the technique could be reliably performed without clinically consequential wire entrapment.

METHODS

This study was conducted using an ex-vivo experimental model with explanted porcine tissue. The study was performed under strict compliance with a protocol approved by the Institutional Animal Care and Use Committee. Porcine GI tissue was chosen because of its similarity to human tissue and because of its well documented use for endoscopic experimental modeling.[11]

Fresh explanted porcine foregut (esophagus, stomach, and duodenum in continuity) was opened longitudinally such that the entire mucosal surface could be accessed (**Figure 1A**). A biopsy punch was then used to create standardized 3-millimeter (mm) diameter full-thickness GI tract defects through the tissue in esophageal, gastric, and duodenal locations. A guidewire was then threaded through the defect and secured to the working surface at a predetermined angle using a surgical clamp. Clips were loaded onto the end of an appropriately sized endoscope for each clip. A Pentax EG2930 diagnostic gastroscope (Pentax Medical, Tokyo, Japan) and an Olympus GIF-2T160 gastroscope (Olympus Corporation, Tokyo, Japan) were utilized. The endoscope was then backloaded over the wire and used to position the OTS-clip over the defect (**Figure 1B, C**). Endoscopic suctioning was used to draw

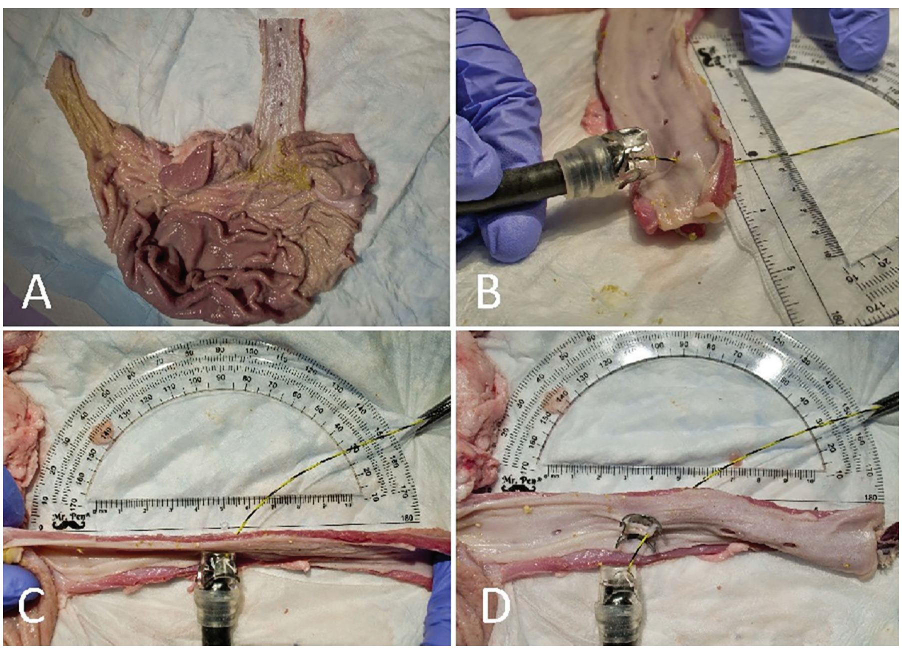

Figure 1. (**A**) The explanted porcine foregut is opened longitudinally to expose the mucosal surface. (**B**) A guidewire is threaded through a three millimeter full-thickness defect made with a biopsy punch. (**C**) The wire is secured at the desired angle and the endoscope and clip are positioned over the defect. (**D**) The over-the-scope-clip is fired over the wire then the wire is withdrawn through the scope, clip, and tissue.

the GI tract wall into the distal cap attachment of the scope and the OTS-clip was fired over the defect and wire in standard fashion (**Figure 1D**).

Immediately following clip deployment, the endoscope was backed away from the clip and the wire was removed through the working channel of the endoscope. The ease of wire removal was graded using a 5-point Likert scale (**Figure 2**). The Likert scale ranged from a score of "1: No difficulty" to "5: Impossible" and the ease of removal was rated by the same individual for the entire experiment.

This process was then repeated for each unique combination of nine OTS-clip types, two wire types, four wire angles, and three tissue locations. Individual clips were reused after each firing and were reloaded onto the OTS-clip deployment device using a clip reloader. Each of nine clip types were fired 24 times each and were individually inspected for defects before reuse. OTS-clips are designed with a superelastic Nitinol composition to withstand reloading and reuse without loss of grip strength. The nine OTS-clip types included 10/3A, 10/3T, 11/6A, 11/6T, 12/6A, 12/6T, 12/6 GC, 14/6A, 14/6T (OVESCO, Teubingen, Germany) representing the entire possible range of clip diameter and teeth shape. The two wire types were 0.035' Jagwire (hydrophilic coated, monofilament kink-resistant nitinol shaft) and 0.035' braided metal guidewire (Boston Scientific, Natick, MA). Four wire angles (0°, 30°, 60°, 90°) were chosen to represent a full range of endoscopic firing positions. The angle was measured between the line of the scope perpendicular to the tissue and the distal wire (**Figure 3**). The three tissue locations were esophagus (4 mm), stomach (6 mm), and duodenum (2 mm) to represent tissues of varying thickness. Statistical analysis was then performed using student's *t* test and analysis of variance. Linear regression was performed using Microsoft Excel. The Likert scale is represented as mean and standard deviation.

Difficulty of Wire Removal Scale
1: No difficulty – wire slides with no resistance
2: Mild difficulty – small amount of resistance is noted, but wire can be slid in continuous motion
3: Moderate difficulty – more resistance is noted, requiring wire to be pulled in noncontinuous motion
4: Extreme difficulty – significant resistance is noted, and significant manipulation of the wire is required to remove
5: Impossible – wire is trapped and unable to be advanced or withdrawn

Figure 2. Likert scale for difficulty of wire removal.

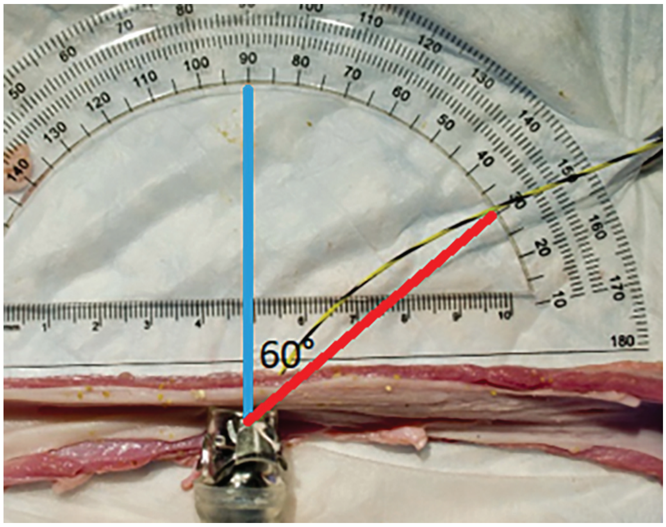

Figure 3. The firing angle of the over-the-scope-clip and wire was measured between the line of the scope perpendicular to the tissue (Blue line) and the distal end of the wire (Red line).

RESULTS

Two hundred sixteen OTS-clip firings with subsequent wire removal attempts were performed (**Table 1**). The mean Likert score for all wire removal attempts was 1.24 ± 00.5 (range 1 – 4, interquartile range = 0). The Likert Score breakdown for all wire removal attempts was as follows: 1 – No difficulty: 174 (80.6%), 2 – mild difficulty: 35 (16.2%), 3 – moderate difficulty: 5 (2.3%), 4 – extreme difficulty: 2 (00.9%), and 5 – unable to remove: 0 (0%).

Table 2 demonstrates the differences in mean Likert scale removal difficulty as calculated for various subgroups. Statistically significant differences were noted in removal difficulty between the nine types of OTS-clip ($P < .05$). When further divided by clip teeth type and clip size, no significant difference was noted between teeth types ($P = .79$) while significant differences were noted between OTS-clip size (10 mm: 1.40 ± 00.7, 11 mm: 1.13 ± 00.3, 12 mm: 1.33 ± 00.6, 14 mm: 1.04 ± 00.2, $P < .05$). No significant differences were noted between wire type, tissue type, or angle ($P > .05$).

Table 1.
Likert Scores of Wire Removal Difficulty

Total Number of attempts	216
Mean Likert Score for all attempts	1.24
Likert Score Breakdown	
1	174 (80.6%)
2	35 (16.2%)
3	5 (2.3%)
4	2 (0.9%)
5	0 (0%)

Figure 4 demonstrates the distribution of the Likert scale removal difficulty rating for every attempt made in this study. The attempts are plotted in the order in which they were performed. The mean Likert score is noted to increase as the number of attempts increases, as demonstrated by the line of best fit (m = 0.002, R^2 = 0.04). As shown in **Table 2**, the mean Likert score for each third of the experimental order significantly increased over the course of the experiment (1st Third: 1.11 ± 00.3, 2nd Third: 1.28 ± 00.6, 3rd Third: 1.32 ± 00.6, P = .04). Notably, all seven attempts with a removal difficult of three or higher occurred in the latter half of the experimental order.

DISCUSSION

In this ex-vivo porcine model study, we deployed OTS-clips over a wire with the goal of determining the safety of the technique by gauging the degree of wire entrapment within the OTS-clip. In a series of 216 unique combinations of OTS-clip types, wire types, deployment angles, and tissue types the guidewire was successfully removed through the endoscope in all cases. In 96.8% of cases, the wire was removed with little or no difficulty while in the remaining 3.2% of cases the wire was still removed in a clinically safe and realistic manner despite some resistance. Given the overall ease of wire removal and the 0% rate of wire entrapment within the clip (which would have been clinically consequential), this study supports the hypothesis that OTS-clip deployment over a guidewire is technically feasible and reliably safe for future clinical implementation. There were statistically significant (but clinically irrelevant) increases in wire removal difficulty with smaller jawed clips (10 mm) compared to larger jawed clips (14 mm).

Since its introduction, the clinical utility of the OTS-clip system has broadened as endoscopists continue to report novel clinical successes of the system including closure of chronic fistula tracts. The surgical management of gastrointestinal tract fistulae is notoriously difficult and associated with significant morbidity, leading to significant interest in endoscopic techniques for fistula closure.[12]

Table 2.
Removal Difficulty (Mean ± Standard Deviation) for Various Experimental Subgroups

Clip Type		
10/3 A	1.58 ± 0.8	p = 0.003
10/3 T	1.21 ± 0.4	
11/6 A	1.08 ± 0.3	
11/6 T	1.17 ± 0.4	
12/6 A	1.33 ± 0.6	
12/6 T	1.42 ± 0.8	
12/6 GC	1.25 ± 0.4	
14/6 A	1.04 ± 0.2	
14/6 T	1.04 ± 0.2	
Clip Teeth Type		
A	1.26 ± 0.6	p = 0.79
T	1.21 ± 0.5	
GC	1.25 ± 0.4	
Clip Size		
10/3	1.40 ± 0.7	p = 0.001
11/6	1.13 ± 0.3	
12/6	1.33 ± 0.6	
14/6	1.04 ± 0.2	
Wire Type		
Monofilament Guidewire	1.19 ± 0.5	p = 0.16
Braided wire	1.29 ± 0.5	
Tissue Type		
Esophagus	1.21 ± 0.4	p = 0.82
Stomach	1.24 ± 0.5	
Duodenum	1.26 ± 0.7	
Angle		
0°	1.22 ± 0.5	p = 0.75
30°	1.30 ± 0.7	
60°	1.19 ± 0.5	
90°	1.24 ± 0.5	
Trial Order		
1st Third	1.11 ± 0.3	p = 0.04
2nd Third	1.28 ± 0.6	
3rd Third	1.32 ± 0.6	

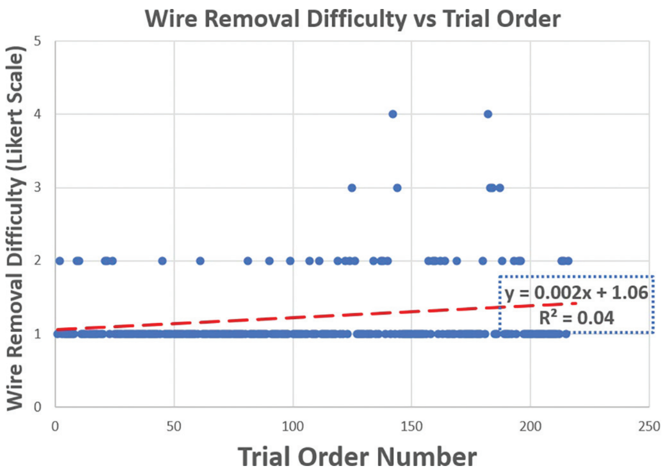

Figure 4. Demonstrates the likert scale of wire removal difficulty in the experimental order in which each trial was performed.

Several large studies have documented the success rate for OTS-clip closure of fistulae to be between 52% and 55%.[3,13] Notably, OTS-clip success for fistula closure is lower than success rates for leak closure and acute defects. To assist in fistula closure, multimodal endoscopic therapy has been demonstrated using adjunctive devices including endoscopic suturing methods and stents.[14,15]

Failure of OTS-clip closure of fistulae is multifactorial and while it is likely strongly related to the underlying disease process and local tissue condition, technical aspects of the clip deployment are also essential for minimizing clinical failure. Ideal OTS-clip deployment relies on the scope, clip, and tissue being aligned in an "end-on" position which can be difficult to achieve depending on the location of the fistula opening within the GI tract. Additionally, accurate fistula identification and precise deployment of the OTS-clip over the defect can be nearly impossible in cases where numerous enteral defects are present such as severe diverticular disease or in cases in which direct visualization of the defect during deployment is compromised by scope position (**Figure 5**). Therefore, the concept of backloading the endoscope and firing an OTS-clip over a wire traversing the fistula tract was proposed and demonstrated in a small case series.[9] However, this raised concerns regarding guidewire entrapment within the clip given several key properties of the OTS-clip. First, the shape-memory effect and high-grade elasticity of the

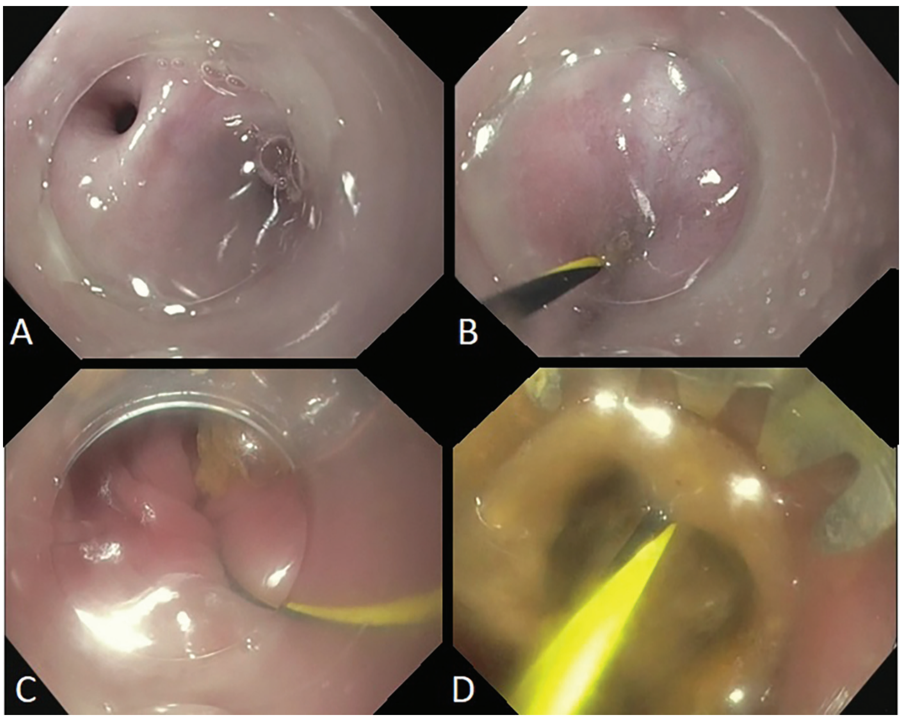

Figure 5. Demonstrates firing an over-the-scope-clip over a wire in a patient with a colovaginal fistula. the fistula could not be identified within the colon but was easily identified by flexible vaginoscopy **(A)** A guidewire was then inserted on the vaginal side of the fistula **(B)** and identified within the colon **(C)**. The wire was backloaded onto the colonoscope, the wire was used to position the clip over the fistula **(D)**, and the clip was subsequently deployed.

nitinol alloy clip leads to a strong continuous closing force that is permanently applied.[16] Further, the OTS-clip system was designed to apply a high mean gripping force across a wide tissue area and studies have shown a gripping force as high as 13.2 Newtons.[17]

Despite the theoretical concern for wire entrapment within the OTS-clip, this experiment was not able to reproduce such a scenario under a wide range of procedural variations including severe wire angulation and braided guidewire. This study did demonstrate modest differences in wire removal difficulty between OTS-clip of varying sizes, but these differences would not be clinically significant and did not represent a meaningful trend such as decreasing difficulty with larger clips. Notably, clip tooth type, tissue type, wire type, and wire angulation did not affect the removal difficulty. Finally, there was a notable trend of increased frequency of more difficult wire removals during the latter portion of the procedure. This trend is most likely explained by the cumulative effect of wire damage from repeat experimentation as the same two wires were used for the entire experiment and minor wire damage was noted towards the end of the experiment. This effect is relevant only to this experimental model and would be unlikely to occur clinically when new wires are used for each case.

In the small number of cases where difficulty was encountered during wire removal, it is important to note that the wire was still removed in a manner consistent with available endoscopic techniques. In this experiment, wire removal difficulty was defined by the resistance of the wire to slide out of the clip while the tip of the endoscope was not in contact with the clip or tissue. However, in all seven cases in which moderate or extreme difficulty was encountered (Likert score 3+), the first maneuver was to advance the endoscope such that the cap attachment was directly opposing the fired clip and tissue. This simple technique provided counter-resistance against the clip and tissue and allowed for the wire to be removed easily in all cases. Although it was not required in this experiment, it should be noted that numerous removal techniques are available to endoscopically remove a fired OTS-clip. A systematic review by Ou et al. published in 2020 cites 18 articles describing various methods for OTS-clip removal including the use of grasping forceps, argon plasma coagulation, a neodymium-doped yttrium aluminum garnet laser, and the remOVE system (OVESCO, Teubingen, Germany).[18] The authors performed a metanalysis of studies evaluating the remOVE system and found a pooled success rate of 89%. This system, which uses resistive heating via direct current pulse to fracture two sides of the clip, would be unlikely to be interrupted in the unexpected event of a wire entrapment.[19] Additionally, the presence of an entrapped wire would be unlikely to interfere with most available removal methods including those mentioned above and other less conventional techniques including guidewire removal and cold saline submersion.[20,21]

The main limitation of this study was that it was conducted in an ex-vivo explanted porcine foregut model. Therefore, the applicability and safety of this technique in all areas of the gastrointestinal tract during actual human endoscopy requires further study. The fibrotic nature and varied defect size of fistula tracts may not be completely represented by the compressible tissue and uniform defect size utilized in this experimental model, which could potentially alter the mechanics of the interaction between the tissue, wire, and OTS-clips. Live animal models could provide further information regarding the safety of firing OTS-clips over a wire at varying angles and defect sizes. Further, only one manufacturer (OVESCO) was studied in this experiment and our results; therefore, cannot be extrapolated to other types of OTS-clips. We believe the evidence presented in this study provide enough preliminary safety data to employ this technique in actual clinical endoscopy cases with the recommendation that diligent recording and reporting of outcomes is performed.

CONCLUSION

This ex-vivo porcine experimental model provides preliminary safety data suggesting that OTS-clips can be fired over a wire under a wide range of procedural variations without evidence of clinically-relevant wire entrapment. This technique can be employed to facilitate OTS-clip closure of GI tract defects when achieving fistula identification or an “end-on” scope position would otherwise be difficult. Further clinical study in human subjects is indicated before wide clinical implementation of the technique.

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