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A Comparison of Thermal Plasma Energy versus Argon Beam Coagulator Induced Intestinal Injury Following Vaporization in a Porcine Model

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Abstract

Objectives—Complete cytoreduction of ovarian cancer often requires excision or ablation of bowel serosa implants. Both argon beam coagulator (ABC) and thermal plasma energy (TPE, PlasmaJet) have been used to ablate bowel serosa implants. Our objective was to identify comparable power settings as well as determine the rate of bowel perforation, depth of thermal injury, and extent of inflammatory response with ABC versus TPE in a porcine model.

Methods/Materials—Nine pigs underwent vaporization of small bowel and colon serosa according to assigned treatment group (TPE versus ABC) and settings (ABC: 30W, 50W, 70W; TPE: Cut 10U, 20U, and 30U and Coagulation 10U, 20U, and 30U). Animals underwent necropsy with blinded histomorphologic evaluation on days 0, 3 and 10 post-procedure to assess for presence of bowel perforation, depth of thermal injury, and extent of inflammatory response.

Results—At necropsy, bowel perforation was not identified in any animals. Depth of treatment with ABC in the porcine colon was variable and unrelated to power settings while TPE was associated with a consistent treatment depth of 1.0mm regardless of location or power. Treatment with ABC resulted in greater tissue coagulation and desiccation as well as increased rates of mucosal necrosis, especially at higher settings (>50W). Treatment with TPE primarily resulted in tissue ablation and minimal mucosal necrosis at low settings (Coag 10–20U). The inflammatory

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The current study reports an off label use of the Plasma Jet device (Plasma Surgical, Roswell, GA).

response associated with TPE treatments were interpreted as biologically benign, and less than that observed with the ABC regardless of treatment settings.

Conclusions—Both ABC and TPE effectively ablate bowel serosa in a porcine model. TPE appears to result in a more predictable tissue effect with less inflammatory response, especially when used at low power settings such as Coag 10U or 20U. These characteristics are appealing for ablation of bowel serosa implants during ovarian cancer surgery and warrant further investigation.

Keywords

ovarian cancer; tumor ablation; cytoreductive surgery

Introduction

The outcome of cytoreductive surgery is one of the most important predictors of survival for patients with advanced ovarian cancer. In patients undergoing primary cytoreductive surgery prior to chemotherapy, complete gross resection of all visible and palpable disease is associated with a significant survival advantage versus patients left with small volume residual disease^(1–4). The proportion of this advantage attributable to tumor biology versus surgeon effort remains uncertain⁽⁵⁾; however, the implication is clear: patients that are able to have all visible disease resected without experiencing a major perioperative complication derive significant benefit from complete gross resection.

While a small percentage of patients with advanced ovarian cancer will achieve a complete gross resection with minimal effort, many patients require extensive surgical procedures to achieve this outcome. In as many as 70% of cases, tumor implants will be found on the surface of the colon or small intestine⁽⁶⁾. Although technically feasible, bowel resection can be associated with a variety of perioperative complications including infection, bowel obstruction, and fistula formation^(7–11). The competing interests of complete gross cytoreduction and minimizing perioperative morbidity are perhaps no more apparent than when a surgeon must decide whether or not to perform multiple bowel resections to achieve no gross residual disease at the risk of potentially increasing postoperative morbidity.

To resolve this conflict, a new treatment strategy that safely allows surgeons to clear bowel serosa without increasing perioperative complications would be ideal. Some authors have reported success using the argon beam coagulator (ABC) to achieve complete gross cytoreduction^(12, 13). Available for more than 30 years, the ABC is a form of non-contact monopolar electrosurgery that is frequently used to dissect and achieve hemostasis in both open and laparoscopic procedures. The ABC has a more uniform distribution of energy and reduces underlying tissue necrosis compared to conventional monopolar energy⁽¹⁴⁾. This uniform energy distribution theoretically slows the depth of injury by arcing the transmitted current away from target areas that have already been treated due to increased tissue resistance that develops as desiccation occurs. Bristow and colleagues reported successful fulguration of small bowel serosa implants using the ABC in selected patients⁽¹²⁾. Unfortunately, several reports of bowel perforation resulting from latent necrosis have also been published^(15–21). It is unclear whether this is a function of the energy source in general or whether specific settings can be identified that result in safe treatment. This uncertainty

has likely prevented the ABC from being more widely used for ablation of tumor on bowel serosa.

The use of thermal plasma energy (TPE, PlasmaJet, PlasmaSurgical, Roswell, GA) to ablate bowel implants has theoretical advantages over the ABC due to its unique tissue energy transfer properties. Unlike the ABC, no electrical current passes through patient tissues with TPE. Instead, low flow argon gas is excited by a low voltage oscillating current applied between internal bipolar electrodes in the handpiece. The resulting high-energy thermal plasma energy emitted by the device has been shown to efficiently ablate soft-tissue by vaporization⁽²²⁾. Despite high peak energy levels, thermal plasma has a low energy-density and quickly dissipates at the site of application, resulting in minimal thermal spread. These properties have led some surgeons to use TPE to ablate superficial and deep endometriosis nodules on the rectum as well as ablate tumor implants in patients undergoing cytoreductive surgery for advanced ovarian cancer^(23–25). There are no data describing optimal settings that confer safe and effective ablation of tumor implants on the bowel using TPE. These settings must be established before TPE can be routinely incorporated into cytoreductive procedures for patients with ovarian cancer.

The objective of the current study is to identify comparable tissue vaporization settings for the ABC versus TPE and assess the risk of latent bowel perforation and/or necrosis in a porcine model. If safety can be demonstrated in this setting, the use of TPE to ablate serosal bowel implants in patients with ovarian cancer undergoing cytoreductive surgery could be better considered.

Materials and Methods

Nine female Yorkshire pigs were evaluated in the study. After induction of anesthesia, the animals were prepped and draped under standard sterile technique. All animals underwent a large vertical midline laparotomy and placement of a self-retaining retractor. All procedures were performed by two surgeons experienced (ET and ED) with the use of both ABC and TPE.

All animals underwent tissue vaporization of the intestines on the same day (Day 0) according to assigned treatment group (TPE versus ABC) and treatment settings (ABC: 30W, 50W, 70W; TPE: Cut –10U, 20U, and 30U and Coagulation - 10U, 20U, and 30U) as outlined in Table 1. Animals underwent a total of 18 – 40 injuries with an equal number of injuries performed on the small intestines and colon. Animals 1 – 3 underwent tissue vaporization with both energy sources at several treatment settings prior to necropsy on either day 0 or day 3. Animals 4 – 9 underwent tissue vaporization with either ABC or TPE at a single treatment setting prior to necropsy on day 10. All treatment sites were demarcated by placement of interrupted non-absorbable 4-0 or 5-0 suture.

For animals 1 – 3, treatment sites were clustered so that escalating treatment settings for each treatment group were spaced approximately four centimeters apart (e.g. one treatment with ABC at 30W, 50W, 70W and 90W, each four centimeters apart). Treatment clusters were spaced evenly along the length of the small intestines and colon. For animals 4 – 9,

treatments sites were spaced at regular intervals along the length of the small intestines and colon. The activation duration (~1 second) and probe distance were kept constant in all applications with a goal lesion diameter of ~1 cm for all lesions. For the ABC, the device was applied at the minimal distance needed to achieve device activation (~5 – 10 mm) while the TPE was applied at a distance close enough to achieve tissue effect according to manufacturer recommendations (~5 mm).

Upon completion of the procedures, all animals except animal 1 were closed using standard closure techniques and a sterile dressing applied. Animal 1 was euthanized approximately four hours after procedure completion for tissue analysis of acute effect. Animals 2 – 9 were recovered from anesthesia and managed according to routine post-operative care for three to ten days according to treatment assignment.

Clinical observations and incision site observations were performed daily. Body weights and body condition scores were recorded prior to surgery and prior to necropsy. Blood samples for clinical pathology analysis were collected prior to injury on Day 0 and prior to necropsy. After euthanasia, animals were subjected to a limited necropsy where all treatment sites were collected, placed into 10% neutral buffered formalin, and processed for histomorphologic evaluation. Additional sites adjacent to injury locations were biopsied when identified to further assess for inflammatory response (i.e. evidence of perforation, peritonitis, or adhesion formation).

Following hematoxylin and eosin staining of paraffin embedded specimens, light microscopy was used to determine histomorphological scoring of parameters that reflected the degree and extent of treatment. Bowel injury was expressed in terms of anatomical layer, as it may be a more clinically relevant measure of depth of injury than absolute measures of depth in millimeters⁽¹⁸⁾. It also avoids errors in measurement associated with contraction of tissue after removal and fixation.

An independent, blinded pathologist (CBSET, Lexington, MA) scored each layer (serosa, outer longitudinal muscularis, inner circular muscularis, submucosa, mucosa) by tissue effect (ablation, desiccation, coagulation, necrosis). Sections were scored as described in Table 2. Ablation and desiccation scores were combined for the inner and outer muscularis to compare intended clinical effect whereas coagulation and necrosis scores were combined as a surrogate for more substantial unintended injury.

Light microscopy of tissue biopsies with features suggestive of an inflammatory response were evaluated to corroborate macroscopic findings suggestive of perforation, peritonitis, or adhesion formation (if present).

Depth of thermal injury was reported as group mean $\pm$ SD. Ordinal histologic data (scores) were reported as group mean $\pm$ SD. The manual tracing and measurement software used for histomorphometry was Olympus MicroSuite Biological Suite (Version 2.5) and Olympus cellSens Dimension Desktop software (Version 1.8). Statistical calculations were generated using R ⁽²⁶⁾.

Results

Evaluation of Acute Tissue Effects

Animal 1 was evaluated for acute tissue effects on the day of treatment. Within the small intestine, the depth of treatment with the ABC device increased with increasing power (see Figure 1). However, within the large intestine, the depth of treatment with ABC was variable with no power related trends. Comparatively, TPE was associated with a fairly consistent treatment depth of 1.0 mm regardless of location (i.e., small vs. large intestine), power (i.e., 10U, 20U, or 30U), or setting (i.e., Cut vs. Coag).

The predominate ABC tissue effect was coagulation and desiccation, especially at higher settings (>50W; see Figure 2). The predominate TPE effect was ablation of tissue in the outer layer of the muscularis and was consistent at every setting tested. Mucosal necrosis was observed with both devices at all settings in the small intestines. The rate of mucosal necrosis increased with higher ABC settings in the colon. No mucosal necrosis was observed with TPE on cut, while a small amount was identified on Coag and was consistent with low power ABC settings (see Supplemental Table).

Microscopic Morphometric Assessment

In Animals 2 and 3 (sacrificed at Day 3), the deepest discernible treatment-related effects of the TPE were primarily within the tunica muscularis/propria (predominately the inner layer), regardless of power or location, and did not extend to the submucosa or mucosa at 10 or 20U power settings (see Figure 3). Comparatively, the ABC exhibited deeper treatment-related effects with routine penetration into the submucosa and mucosa, particularly with increased power settings in the large intestine. Complete transmural penetrance was observed in two 50W ABC sites (one each in small and large intestine) and both 70W large intestine sites.

By Day 10 (animals 4 – 9), discernible treatment effect and penetration was more variable, regardless of treatment. TPE was associated with an increased incidence of penetration into the submucosa, relative to Day 3. However, evidence of mucosal penetration was limited to the TPE setting of 30U, the highest setting tested, with only one incidence of complete transmural penetrance in the small intestine. Regardless of treatment group or time point, there was no evidence of frank perforation.

Microscopic evaluation revealed that treatment of small and large intestinal tract serosa with TPE resulted in consistently effective and focally delineated removal of the treated tissue with no evidence of locally adverse effects (e.g., perforation, peritonitis, restrictive adhesions). In addition, the nature and magnitude of the tissue response associated with areas of TPE treatment were interpreted as biologically benign, and less than that observed with the ABC, especially at low power settings (see Figure 4).

All animals tolerated the treatment procedures and survived to the scheduled necropsy time point (days 0, 3, and 10). Observations other than normal were limited to transient clinical signs mainly of decreased appetite and vomiting, which resolved generally by Day 6, and were not specifically related to device type or power setting.

Discussion

Achieving a complete gross resection is one of the most powerful predictors of survival in patients undergoing primary cytoreduction for advanced ovarian cancer. The development of a tool that can safely and effectively ablate bowel serosa implants could facilitate a greater proportion of patients achieving this important outcome. Our results demonstrate that both the argon beam coagulator (ABC) and thermal plasma energy (TPE, PlasmaJet) devices appear to ablate the serosa of the porcine small bowel and colon without resulting in bowel perforation when used at low power settings. TPE appears to have the added benefit of consistently ablating superficial layers without causing damage to underlying structures, especially if used at the lowest coagulation settings of 10 – 20U. On the other hand, ABC requires higher energy settings to achieve similar ablation effects seen with the TPE, at the expense of increasing coagulation and necrosis of deeper layers. We were unable to identify comparable tissue settings for the ABC that resulted in similar depth of ablation as the TPE without significantly increasing destructive effects on deep tissues. These results suggest that the therapeutic range of the TPE may be superior to the ABC for ablation of bowel implants especially when low TPE power settings (Coag 10 – 20U) are utilized.

Avoiding injury to deep bowel wall layers, especially the mucosa, is a critical requirement for successful application of ablative techniques to remove bowel serosa implants in patients with advanced ovarian cancer. This is due to the catastrophic impact that deep injury and resultant bowel perforation can have on perioperative morbidity and long term mortality^(27, 28). This effect is compounded when injury is unrecognized at the time of the procedure^(29, 30). As ablation with the ABC may result in deep injury that cannot be directly visualized, the risk of delayed perforation would seem to be higher with this technique. When coupled with a previous report suggesting a narrow range of lateral thermal damage, the effect of TPE appears to be more predictable than ABC⁽²²⁾. Although our results did not demonstrate an increased rate in perforation with the ABC versus TPE, tissue effects with TPE may translate into a lower risk in iatrogenic bowel injury in ovarian cancer patients with further study. As porcine small bowel is considerably thinner than human small bowel (2 versus 3 mm), it is possible that the risk of perforation in human bowel may be even lower if used in a similar fashion as in the current protocol.

In addition to a theoretically lower risk of bowel perforation in humans, TPE appears to also be associated with equivalent, if not reduced, inflammatory response in the porcine model versus ABC. Inflammation is a necessary component of wound healing but has a number of secondary deleterious effects including adhesion formation^(31–33). Our results suggest equivalent, if not lower, rates of microscopic inflammatory response with TPE at low power settings versus ABC. While this did not correlate into objective changes in recovery between porcine subjects, the recovery of human patients recovering from cytoreductive surgery is likely more complex and nuanced than what could be assessed in the current study. The potential for reduced inflammatory response with TPE could be an added benefit if evaluated in human subjects.

These results suggest the potential utility of TPE to ablate bowel implants in human subjects. Low power settings (Coag 10 – 20U) appeared to be safe and effective in our

porcine model and should be considered as the standard for further evaluation. At this time, only a small case series has been published evaluating the utility of TPE in this setting⁽¹³⁾. These results must be replicated prior to broader application. More importantly, tissue effects could be further evaluated in ovarian cancer patients undergoing cytoreductive surgery to confirm any potential advantages with respect to clinical outcomes and to answer the questions of safety and efficacy in this setting.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Figure 2.

Figure 3.

Figure 4.

Table 1

Treatment Assignments for Porcine Tissue Ablation Comparison of Argon Beam Coagulator versus Thermal Plasma Energy

Animal	Necropsy Time Point	Treatment	Settings	Treatment Sites (Small Intestine, Large Intestine)
1	Day 0	TPE	CUT 10, 20, 30 COAG 10, 20, 30	24 Total, 4 per setting (2, 2)
		ABC	30W, 50W, 70W, 90W	16 Total, 4 per setting (2, 2)
2	Day 3	TPE	COAG 10, 20, 30	18 Total, 6 per setting (3, 3)
3		ABC	30W, 50W, 70W	18 Total, 6 per setting (3, 3)
4	Day 10	TPE	COAG 10	20 Total, one setting (10, 10)
5			COAG 20	20 Total, one setting (10, 10)
6			COAG 30	20 Total, one setting (10, 10)
7		ABC	ABC 30W	20 Total, one setting (10, 10)
8			ABC 50W	20 Total, one setting (10, 10)
9			ABC 70W	20 Total, one setting (10, 10)

ABC: Argon beam coagulator, TPE: Thermal plasma energy (PlasmaJet)

Table 2

Histomorphology Scoring Matrix

Score	Microscopic Changes (0 – 3)
0	No observable change
1	Minimal – a nearly imperceptible feature/change in the tissue
2	Mild/moderate – an easily identifiable and/or notable feature/change in the tissue
3	Marked/severe – prominent to overwhelming feature/change in the tissue