This paper presents the opinion of Dr. Craig E. McCoy, DO FACOG FPMRS. Bovie Medical Corporation's J-Plasma® electrosurgical generators and hand pieces are indicated for the delivery of helium gas plasma to cut, coagulate, and ablate soft tissue during open and laparascopic surgical procedures. The safety and effectiveness of J-Plasma® for the treatment and prevention of intra-abdominal adhesions has not been established. Dr. McCoy is a paid consultant to Bovie Medical Corporation.

White Paper

J-PLASMA'S ROLE IN TREATING AND PREVENTING INTRA-ABDOMINAL ADHESIONS

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Introduction

Abdominal adhesions the silent, expensive byproduct of surgical procedures

Abdominal adhesions are fibrous, sometimes vascular bands of scar tissue that form between organs or tissues in the abdomen.[1] The adhesions' ability to limit the normal mobility and function of intra-abdominal organs appears to be the main source for their pathology. Injury to or inflammation of a serosal surface generally initiates the formation of adhesion.[2] This complex process activates the inflammatory immune cascade that ultimately leads to the laying down of fibrin strands, if degradation does not occur in a timely manner. Mesothelial cells are the key mediators of matrix remodeling through their response to mechanical, physical, and chemical signaling.[3] The mesothelium appears to be a major source of peritoneal fibrinolytc activators [4,5] and plays a central part in adhesion formation.

The formation of postoperative abdominal adhesions is a major cause of morbidity, resulting in multiple complications many of which manifest years later.[6,7] Total costs related to adhesions have been estimated to be 1.2 billion U.S. dollars per year in the U.S.[8] Menzies and Ellis found that 93% of patients who had undergone one or more previous surgeries had intra-abdominal adhesions.[9] It was reported that 5.7% of the hospital readmissions after any kind of previous abdominal surgery were directly related to adhesions and 3.8% of these admissions were treated by laparotomy to correct the problem of the formed adhesions.[10]

Previous gynecologic surgery is the second most common cause of adhesive small bowel obstruction after colorectal surgery.[10, 11,12,13] Moderate to severe adhesions may be responsible for 40% of infertility.[14] A prospective study revealed that 200 (82%) of 224 patients suffering from chronic pelvic pain had only adhesions and no other disease; they underwent primary laparoscopic adhesiolysis and three months after adhesiolysis, 74% of the patients were pain free or had less pain.[15]

Challenge

Methods of adhesion prevention

In terms of clinical interventions, adhesion prophylaxis is a very appealing therapeutic target since the window of time for a successful intervention is relatively small (in the order of 5-7 days).[3] The main prevention strategies for surgical adhesions are:

- **Pharmacologic agents strategies** target the immune response to adhesion formation, yet contain a long list of failed agents including corticosteroids, antihistamines, dextran, saline, anti-cytokine agents, recombinant tissue plasminogen activators, aprotinin, octreotide and heparin.[16,17]
- **Barrier strategies**, such as Interceed, are believed to prevent adhesions by offering an inert and inactive barrier to cellular adhesion, since the constituent of this material does not appear to alter the signaling or behavior of mesothelial cells directly.[18] Ideally, such a barrier should be anti-adhesive, highly

biocompatible, resorbable, adherent to traumatized surfaces, effective on an oozing surface, applicable through the laparoscope, and relatively inexpensive. As yet, such an ideal barrier does not exist.[19]

Additionally, the data is not overwhelming for the use of barrier products for prevention of adhesions and has been criticized due to the added cost to health care. In fairness, Wilson et. al. estimated that between 5,686 and 7,766 patients would be necessary to evaluate adhesion over the escalating economic burden of health care, particularly in the United States. Straight forward prevention from a cost-effectiveness perspective in a randomized prospective trial, such that completion of such a rigorous study would be difficult at best.[20]

- **Surgical intervention strategies** have focused mainly on limiting tissue injury by avoiding powdered gloves, minimizing tissue handling, avoiding desiccation of tissues, and other modification to the surgical technique that might decrease trauma.[1] Interestingly, when the surgical trauma of laparotomy is reduced to a laparoscopic approach, experimental tumor growth has been shown to be significantly attenuated.[21,22] The reduction in tumor growth seems to be due to a less pronounced immune dysfunction after the reduced surgical trauma.[23]

Current surgical strategies lack proactive prevention

Despite the known burden of adhesions, both surgeons and health care administrators remain unconvinced that the current evidence for adhesion prevention products warrant routine use.[20] Kaptanoglu et.al state the most effective means of limiting adhesions is by using an appropriate surgical technique that includes gentle tissue handling, gentle dissection, meticulous hemostasis avoidance of extensive thermal injury, adequate irrigation, avoidance of foreign bodies such as powdered gloves and non-absorbable suture materials, and prevention of infection.[24] Since laparoscopic procedures result in a more gentle manipulation of tissues, lower bleeding, and lower contamination with foreign bodies then conventional "open" surgery, there have been many claims made that laparoscopy also reduces the incidence of postoperative adhesions. [25] The literature clearly supports these claim; however, the fact remains that adhesions still occur.

The question still unanswered is why? Many factors may influence the development of adhesions, including mechanical trauma, chemical irritation, drying of the serosa, bleeding into the abdominal cavity, ischemia, infection, and foreign materials,[2] with mechanical injury and tissue ischemia playing pivotal roles. Plus, in addition to thermal injury caused by surgical instruments such as electrocautery and laser equipment, factors such as tissue dryness, crushing, and clamping are thought to cause or facilitate adhesion formation.[26] Amaral and coworkers performed laparoscopic cholecystectomies on pigs to evaluate postoperative adhesion formation caused by different surgical instruments. They reported that the incidence of adhesions caused by harmonic, electrocautery, and laser surgery were 22%, 67%, and 78% respectively, and assumed the differences resulted from the degree of tissue damage caused by each energy source. They concluded surgical instruments can be selected to reduce postoperative adhesion formation.[27]

The need exists for an innovative surgical option, both technique and instrumentation that offers minimal tissue injury and further reduces adhesions formation while delivering safe, effective, and long lasting patient outcomes.

The Solution

J-Plasma® from Bovie Medical Corporation is a new FDA-cleared electrosurgical device harnessing the power of helium gas plasma for precise and controlled treatment of soft tissue. This groundbreaking multi-modal electrosurgical instrument is an alternative to traditional monopolar, bipolar, or laser devices. J-Plasma allows surgeons to probe, scalpel, fulgurate, coagulate, dissect, ablate and paint diseased tissues in continuous or pulsed modes, without grounding pads, eye protection, wet surgical drapes, or calibration procedures in both open and laparoscopic surgery.[28]

The use of nonconductive currents limits direct injury and tissue spread and reduces the risk of direct and capacitive coupling. Additionally, J-Plasma allows for excision or ablation of abdominal adhesions with controlled precision and reduced fear of injury to adjacent vital organs or tissues. With virtually no thermal flow or collateral tissue damage, surgeons are afforded a new, innovative surgical tool for tackling abdominal adhesions.

Table 1.0 provides a comparison of existing surgical energy modalities available to gynecologists. The following identifies variable differences in the devices and their use in surgery.

Table 1.0 - Surgical Energy Modality Comparison

Modality	Energy Source	Thermal Flow Conduit	Thermal Spread Collateral	Energy Control
J-Plasma®	Helium Plasma (RF)	Plasma Envelope (Tissue Surface)	0.2mm per side[36]	Continuous or Pulsed
Monopolar Pencil	Electrosurgical Generator (RF)	Direct Contact (i.e. electrode) (Tissue Current Density Heating)	8.5mm (mean width) [33]	Continuous
Ultrasonic/Harmonic	Frictional Heat (High-frequency/Mechanical)	Direct Contact (Tip / Tissue Frictional Interface)	2-3mm per side of the jaws[37]	Continuous or Pulsed
CO_2 Laser	Highly Concentrated Light Emission (Gas Excitation)	Concentrated Light (Target Tissue Surface Heating)	0.3mm per side[38]	Continuous or Pulsed
Argon Plasma (Argon Beam Coagulator)	Argon Plasma (RF / Monopolar)	Plasma Envelope (Tissue Surface & Deeper to Pad)	1.4mm per side[39]	Continuous
Electrocautery	Direct Current / Device Resistive Heating	Direct Contact	*varies*	Continuous

The Results

My career as a gynecologic surgeon has spanned over 20 years. It is rare not to encounter some form of adhesions when performing laparoscopy for female pelvic pain. Although I would agree that adhesions in and of themselves do not cause pain, their ability to restrict movement and function does. A logical step is to remove any adhesions when feasible in a manner that will reduce recurrent adhesion formation. To date, satisfactory barrier methods do not exist that significantly reduce adhesions without adding to the economic burden on the health care system.

Viewing surgical instrumentation as an alternative to reduced adhesion formation has been stagnant due to the lack of alternative energy sources availability over the past decade. This has changed now with Bovie's J-Plasma. Tissue studies support that its precise application results in minimal lateral and depth of spread. The ability to apply this energy in a cutting manner with reduced bleeding and tissue ischemia prompted me to implement this device in my practice over two years ago. I have seen, anecdotally, a lengthened pain free interval and increased patient satisfaction in those patients treated with J-Plasma. For those patients that a second procedure was necessary, fewer adhesions were seen.

In my practice, J-Plasma has proven to be a safe, precise, and economical tool for treating pelvic and abdominal adhesions. I hypothesize the differentiator impacting adhesion formation and its reoccurrence in my practice is the J-Plasma for the following reasons:

Minimally invasive approach

Experimental and clinical studies have brought evidence that surgical trauma markedly affects the immune system, including both the specific and the non-specific immune response.[29] Probably the most successful way to reduce surgical trauma-induced immunosuppression is to reduce the extent of trauma. This is achieved by careful operation; however, it may imply the use of a minimally invasive approach including laparoscopic surgery.[30,31,32]

Minimal, but directed energy

Minimal energy is required for adhesiolysis with J-Plasma. My preferred settings are 20% power with 4 Liters of flow. I extend the blade or needle point approximately 2 mm and begin the process of reducing the adhesions in the standard laparoscopic microsurgical technique. The energy is directed in front of the tip and allows for direct visualization. It is easy to see that no escar forms and minimal if any lateral tissue injury occurs. (To view videos of J-Plasma used to perform adhesiolysis, go to www.boviemedical.com). J-Plasma avoids the explosive effect of monopolar electrosurgery energy.

Minimal lateral and depth spread

With J-Plasma, as with all surgical energy devices, the lateral spread of the instrument depends on multiple factors. With the typical default settings, the J-Plasma energy has a maximum depth of spread of about 2mm and a maximum lateral spread of about 4mm. In comparison, Sutton et. al demonstrated that the monopolar pencil has a depth of thermal damage of 4.75mm with mean with of spread of 8.5mm at 20w/10w pure coagulation[33]. This would support that less surgical injury is occurring with J-Plasma and would meet one of the suggested criteria for the reduction of adhesions.

Cold Plasma

Another proposed source for adhesion formation is infection. Although the infection rate is reduced with laparoscopy, it has to be assumed that some bacteria are introduced into the abdominal cavity at the time of surgery. Researchers discovered that bacteria cannot cope with the harsh environment created by plasma; bacteria died in large numbers in a matter of minutes and even seconds depending on the strength of the bacterial strain.[34] The ability of plasma to kill bacteria cells and to accelerate the proliferation of specific healthy tissue cells , known as the "plasma kill/plasma heal" process, has led scientists to investigate the use of cold plasma for wound care.[34] This may prove in the future to be a benefit of using cold plasma in laparoscopy. Jacobi et al[35] did a study that looked at adhesion prevention. In one of their study arms, they used helium for insufflation and found a lower postoperative adhesion scores when compared to open procedures or laparoscopy using CO2 gas. They theorize this to be secondary to the antibacterial effects related to helium. The J-Plasma electrosurgical device works by passing inert helium gas through an electrically-charged retractable surgical blade to create cold plasma.

Conclusion

Abdominal and pelvic adhesions have the potential to cause significant morbidity and in some instances mortality. The economic burden on the health care system is apparent. Prevention of adhesion-related morbidity offers a real opportunity for cost savings in health care expenditures,[19] as well as improved patient outcomes. Additionally, current studies and firsthand experience strongly support that the unique properties of J-Plasma appear to contribute to the prevention of abdominal adhesions. The device's ability for reduced lateral or depth of energy spread directly limits the trauma to the local tissue. Additionally, the device does not require any crushing mechanism to be effective nor does it have a drying effect on tissue. The antibacterial effect of the plasma, as well as free Helium gas, is yet to be determined; however, preliminary laboratory studies are showing promise. Future clinical studies may determine whether the use of J-Plasma as an energy source in laparoscopic surgery results in less postoperative adhesions.

References

1 Liakakos T, Thomakos N, Fine PM, Dervenis C, Young RL. Peritoneal adhesions: Etiology, pathophysiology, and clinical significance. Recent advances in prevention and management. Dig Surg 2001;18:260-73

2 Ozel H, Avsar F, Topaloglu S, Sahin M. Induction and assessment methods used in experimental adhesion studies. Wound Rep Reg 2005;13:358-364

3 Boland G, Weigel R. Formation and prevention of postoperative abdominal adhesions. J. Sur Res 2006;132:3-12

4 Van Hinsberg VWM, Kooistra T, Scheffer MA, Hajo van Bockel J, van Muijen GN. Characterization and fibrinolytic properties of human omental tissue mesothelial cells. Comparison with endothelial cells. Blood 1990;75:1490-7
5 Ivarsson ML, Holmdahl L, Falk P, Molne J, Risberg B. Characterization and fibrinolytic properties of meothelial cells isolated from peritoneal lavage. Scand J Clin Lab Invest 1998;58:195-203
6 Parker MC. Epidemiology of adhesions: the burden. Hosp Med 2004;65:330
7 Jeekel H. Cost implications of adhesions as highlighted in a European Study. Eur J Surg Suppl 1997;579:43
8 Becker JM, Dayton MT, Fazio VW, et al. Prevention of postoperative abdominal adhesions by sodium hyaluronate-based bioresorbable membrane: A prospective, randomized, double blind multicenter study. J Am Coll Surg 1996;183:297-306
9 Menzies D, Ellis H. Intestinal obstruction from adhesion-how big is the problem? Ann R Coll Surg Engl 1990;72:60-3
10 Ellis H, Moran BJ, Thompson JN, et al. Adesion-related hospital readmissions after abdominal and pelvic surgery: A retrospective cohort study. Lancet 1999;353:1476-80
11 Wilson MS, Hawkswell J, McCLoy RF. Natural history of adhesional small bowel obstruction: counting the cost. Br J Surg 1998;85:1294-8
12 Miller G. Boman J, Shrier I, Gordon PH. Natural history of patients with adhesive small bowel obstruction. Br J Surg 2000;87:1240-7
13 Williams SB, Greenspon J, Young HA, Orkini BA. Small bowel obstruction: conservative vs. surgical management. Dis Colon Rectum 2005;48:1140-6
14 Vrijlad WW, Jeekel J, Geldorp HG, Swank DJ, Bonjer HJ. Abdominal adhesions: intestinal obstruction, pain, and infertility. Surg Endosc 2003;14
15 Swank DJ, Van Erp WF, Van Repelaer Driel OJ, Hop WC, Bonjer HJ, Jeekel H.) A prospective analysis of predictive factors on the results o laparoscopic adhesiolysis in patients with chronic abdominal pain. Surg Laporsc Endosc Percutan Tech 2003;13:88-94
16 Oncel M, Remzi FH, Senegore AJ, Connor JT, Fazio VW. Comparison of novel liquid (Adcon-P) Sodium hyaluronate and carboxymethylcellulose membrane (Seprafilm) postsurgical adhesion formation in a murine model. Dis Colon Rectum. 2003;46:187-97
17 Hellebrekers BW, Trimbos-Kemper GC, van Bitterswijk CA, Bakum EA, Trimbos JB. Effects of five different barrier materials on postsurgical adhesion formation in the rat. Hum Repro. 2000;15:1358-63
18 Gago LA, Saed GM, Wang RX, et Al. Effects of oxidized regenerated cellulose on the expression of extracellular matrix and transforming growth factor-beta 1 in human peritoneal fibroblasts and mesothelial cells. Am J Obstet Gynecol 2003;189:1620, discussion 1625
19 Bristow RE, Santillan A, Diaz-Montes TP, Gardner GJ, Giuntoli RL 2nd, Peeler ST. Prevention of adhesion formation after radical hysterectomy using a sodium hyaluronate/carboxymethylcellulose (HA-CMC) barrier: A cost-effetiveness analysis. Gynecol Oncol 2007;104:739-46
20 Woilson MS, Menzies D, Knigt AD, Crowe AM. Demonstrating the clinical and cost effectiveness of adhesion reduction strategies. Colorectal Dis 2002;4:355-60
21 Da Costa ML, Redmond HP, Finnegan N, Flynn M, Bopuchier-Hayes D. Lapratomy and laparoscopy differentially accelerated experimental flank tumour grouth. Br. J Surg 1990;85: 1439-1442
22 Allndorf JD, Bessler M, Kayton ML, Oesterling SD, Treat MR, Nowygrod R, Whelan RL.Increased tumor establishment and growth after laparotomy vs laparoscopy in a urine model. Arch Surg 1995;130: 649-653
23 Allendorf JD, Bessler M, Horvath KD, Marvin MR, Laird DA, Whelan RL. Increased tumor establishment and growth after open vs laparoscopic surgery in mice may be related differences in postoperative T-cell function. Surg Endosc 1999;13:225-233
24 Kaptanoglu L, Kueuk H, Yegenoglu A, Uzun H, Eser M, Mentes C, Kurt N. Effects of Seprafilm and Heparin in combination on intra-abdominal adhesions. Eur Surg Res 2008;41"2-3-207
25 Gutt CN, Oniut, Schemmer P, Mehrabi A, Buchler W. Fewer adhesions induced by laparoscopic surgery? Surg Endosc 2004;18:898-96
26 Stringer NH. Laparoscopic myomectomy with the Harmonic Scalpel: a review of 25 cases. J Gynecol Surg 1994;10:241-245
27 Amaral JF, Chrostek C. Comparison of the ultrasonically activated scalpel to eletrosurgery ad laser surgery for laparoscopic surgery. Surg Endosc 1993;7:141
28 Pedroso J, Gutierrez M, Volker W. J-Plasma, Monopolar pencil, Argon Beam and CO2 laser electrosurgery: Comparative evaluation of thermal spread in a porcine tissue model. White paper 2014
29 Menger M, Vollmar B. Surgical trauma: hyperinflammation versus immunosuppression?Arch Sur 2004;389:475-484

30 Widhirt SM, Schulze C, Schulz C, Egi K, Brenner P, Mair H, Schutz A, Reichart B. Reduction of systemic and cardiac adhesion molecule expression after off-pump versus conventional coronary artery bypass grafting. Shock 2001;16(suppl 1):55-59
31 Sietses C, Beelen RH, Meiger S, Cuesta MA. Immunological consequences of laparoscopic surgery, speculations on cause and clinical implications. Lanenbecks Arch Surg 1999;384:250-258
32 32 Decker D. Springer W. Decker P, Tolba R, REmig J, Strunk H, Hirner A, van Ruecker A. Changes in TH1/TH2 immunity after endovascular and conventional infrarenal aortic aneurysm repair: it's relevance for clinical practice. Eur J VAsc Endovasc Surg 2003;25:254-261
33 Sutton C AJ. History of power source in endoscopic surgery. J Minim Invasive Gynecol. May Jun 2013 20(3):271-8
34 Laroussi M, Kong MG & Morfill G, (Eds.) Plasma medicine: applications of low-temperature gas plasmas in medicine and biology. Cambridge University Press 2012;
35 Jacobi CA, Sterzel A, Braumann C, Halle E, Stasslein R, Krahembuhl L, Muller JM. The impact of conventional and laparoscopic colon resection (CO2or helium) on intraperitoneal adhesion formation in a rat peritonitis model. Surg Endosc 2001;15:380-386
36 Data on file at Bovie Medical Corportion
37 Emam TA1, Cuschieri A . How safe is high-power ultrasonic dissection? Ann Surg Feb 2003;237(2):186-91
38 Hanby DF1, Gremillion G, Zieske AW, Loehn B, Whitworth R, Wolf T, Kakade AC, Walvekar RR. Harmonic scalpel versus flexible CO2 laser for tongue resection: a histopathological analysis of thermal damage in human cadavers. World J Surg Oncol. Aug 1 2011;9:83. doi: 10.1186/1477-7819-9-83
39 Data on file at Bovie Medical Corportion