

## To Whom It May Concern,

If invasive endometriosis is left untreated, there is a significant risk that the patient's symptoms will persist despite surgery with an ongoing impact on the patient's quality of life and a need for further intervention.<sup>1-2</sup> In order to address pelvic pain associated with endometriosis, minimize risk of recurrence and avoid a need for further surgery, all areas of disease should, therefore, be treated during the patient's index surgery. Endometriosis may be treated surgically by destroying the lesions with thermal energy (fulguration/diathermy/cautery/coagulation and ablative vaporization) or by resecting the lesions to healthy margins (wide excision). Table 2 provides a comparative synopsis of the efficacy of these three surgical treatment modalities commonly used in the management of superficial (peritoneal) and invasive (retroperitoneal) endometriosis as reflected in the medical literature.

*Table 2: Efficacy of treatment modalities in the surgical management of endometriosis.*

		<b>TREATMENT METHOD</b>		
		<b>Fulguration/diathermy/ cautery/coagulation</b>	<b>Ablative vaporization</b>	<b>Wide excision</b>
<b>Treatment efficacy:</b>	<b>Peritoneal disease</b>	<p>Research examining the efficacy of fulguration (mono-polar and bipolar coagulation) in the eradication of peritoneal endometriosis in female patients has found that disease persists despite treatment in 80.8% and 90.4% of lesions following monopolar and bipolar coagulation respectively.<sup>3</sup> Fulguration is therefore not a reliable means of eradicating even superficial endometriosis.</p> <p>Fulguration does not allow for biopsy confirmation of the pathology of the tissue, it can only be consistently applied to small surface areas (not diffuse areas of disease) and to areas of disease that are not overlying vital structures, such as the ureters.<sup>4</sup></p>	<p>Research examining the efficacy of ablative vaporization with the CO<sub>2</sub> laser in the eradication of peritoneal endometriosis in female patients has found that disease persists despite treatment in 28.9% of lesions.<sup>3</sup> While ablative vaporization is considerably more effective than fulguration, many patients treated with ablative vaporization are likely to experience incomplete eradication of their disease especially given multiple areas of involvement are present in most cases.<sup>7</sup></p> <p>Ablative vaporization of mild to moderate endometriosis has been found to be more effective in alleviating pelvic pain than diagnostic laparoscopy alone (no treatment)<sup>8</sup>.</p> <p>As with fulguration, ablative vaporization does not allow for biopsy confirmation of the pathology of the tissue, and can only be consistently applied to small surface areas (not diffuse areas of disease).<sup>4, 20</sup></p>	<p>Excision is the only method of treatment of endometriosis that enables complete removal of the disease.<sup>3</sup> The concept of wide excision is supported by the literature on the grounds that recurrence of disease most commonly occurs at or proximal to the sites of previous treatment, suggesting that the initial area of resection was not wide enough. By utilizing wide excision, the risk of leaving undetected endometriosis is minimized.<sup>14</sup> Unlike, fulguration and ablative vaporization, excision allows the surgeon to assess the full extent of disease; the breadth and depth. Simply differentiating between peritoneal and retroperitoneal disease can be challenging without performing excision.<sup>20</sup></p> <p>Excision of endometriosis has been found to be effective in both eradicating the disease, reducing symptoms across multiple domains, and improving quality of life.<sup>15-21</sup> In the majority of patients, the benefits of excision persist during long-term follow-up.<sup>46-48</sup> Reoperation rates following excision are low and only a minority of patients are found to have disease recurrence despite long-term follow-up.<sup>16,18</sup></p>

				<p>When disease recurrence does occur, the disease is typically milder and subtler than at the index surgery.<sup>16</sup></p> <p>Excision can be applied to any area of the pelvic peritoneum regardless of underlying structures. It enables biopsy confirmation of the pathology.<sup>3,20</sup></p>
	<b>Retroperitoneal disease</b>	<p>Unknown.* No studies have yet explored the methodology, safety, or the efficacy of fulguration (diathermy, cautery, coagulation) in the treatment of retroperitoneal endometriosis. It is unclear how fulguration could be safely or effectively applied in the treatment of retroperitoneal endometriosis due to the effects of thermal spread on surrounding tissue associated with this technique and the proximity of vital structures to retroperitoneal endometriosis. Case reports have, however, been published of complications arising from undetected thermal injury secondary to fulguration of pelvic endometriosis.<sup>5</sup></p> <p>* Posadzka and colleagues (2015) studied the effects of <i>electroablation</i> in the treatment of invasive endometriosis but due to a lack of detail explaining the treatment, it is unclear whether their treatment refers to fulguration or vaporization. The study found both laser and electroablation failed to relieve pelvic pain across multiple domains at 6 months post-surgery.</p>	<p>Limited research has been undertaken into the efficacy of ablative vaporization in the treatment of invasive endometriosis. Of the research published to date, the findings have been mixed. While Jones and Sutton (2003) reported reduction in pain across all domains at 1 year post-op, a more recent study by Posadzka and colleagues (2015) found the benefits of CO<sub>2</sub> laser ablation to be limited to a reduction in dysmenorrhea while other forms of pelvic pain failed to show long-term improvement.<sup>9</sup> Interestingly, Jones and Sutton (2003) found dysmenorrhea to be the symptom that responded least well following this intervention. On average, patients reported ongoing pain across all domains despite a degree of improvement. The results are further complicated by the fact that nearly a third of the patients in their study were receiving concurrent ovarian suppressive therapy. The efficacy of ablative vaporization in the treatment of invasive endometriosis therefore remains unclear.</p>	<p>Excision of deep endometriosis has been studied extensively.<sup>e.g.15-21</sup> It has been found to be effective in managing all aspects of retroperitoneal disease with low recurrence rates following complete excision<sup>16,18,21</sup>, and acceptable complication rates given the complexity of the surgery and the severity of debilitation experienced prior to treatment.<sup>18</sup></p> <p>Unlike other approaches (fulguration and ablative vaporization), the approach to the treatment of retroperitoneal endometriosis via excision has been described in detail and is well established in the medical literature.<sup>e.g. 22</sup></p>
<b>Comparison of outcomes:</b>	<b>Peritoneal disease</b>	<p>No prospective clinical comparison studies exist between fulguration of endometriosis and other surgical techniques. Higher rates of post-operative adhesions have been reported in a rat model following fulguration of peritoneal endometriosis when compared to excision.<sup>6</sup></p>	<p>Several studies have compared the efficacy of ablative vaporization and excision in the management of peritoneal endometriosis.<sup>11-13</sup> Of these studies, Healey and colleagues (2014) provided the longest follow-up and found that at 5 years post-treatment, women who underwent ablative vaporization had less relief of dyspareunia and were more likely to require ovarian suppressive therapy for the ongoing management of endometriosis-associated pelvic pain than women who had received excision surgery.</p>	
	<b>Retroperitoneal disease</b>	<p>No relevant studies.*</p> <p>See comment above regarding the study by Posadzka and colleagues (2015) comparing “electroablation” and laser ablation.</p>	<p>No relevant studies except for the aforementioned study that compared laser ablation with “electroablation”. There are no published data comparing ablative vaporization with excision of invasive (retroperitoneal) endometriosis.</p>	<p>No studies have been conducted comparing excision of retroperitoneal disease with other surgical techniques. When compared to placebo control, excision has been found to be an effective treatment of invasive endometriosis across</p>

				multiple symptom domains. <sup>21</sup> Excision is the only mode of treatment for which its efficacy in treating all forms of retroperitoneal endometriosis (urinary, intestinal, diaphragmatic) has been investigated and is established. <sup>22-25</sup> It is therefore considered the gold standard in the treatment of invasive endometriosis and should be the mode of surgical treatment for patients presenting with advanced endometriosis.
--	--	--	--	--

While endometriosis is a common disease, its effective surgical treatment poses significant challenges that require extensive knowledge and surgical expertise.

### References

1. Angioni, S, et al. (2015). Pain control and quality of life after laparoscopic en-block resection of deep infiltrating endometriosis (DIE) vs. incomplete surgical treatment with or without GnRHa administration after surgery. *Arch Gynecl Obstet*, 29;363-370.
2. Cao, Q, et al. (2015). Comparison of complete and incomplete excision of deep infiltrating endometriosis. *Int J Clin Exp Med*, 15;21497-21506.
3. Fulop, IJ, et al (2013). Evaluation of the efficacy of the different operative techniques in the treatment of peritoneal endometriosis. *J Min In Gynecol*, 20;S6-S7.
4. Redwine, DB (2005). Redefining endometriosis in the modern era. *Leadership Medica; on-line*.
5. Steckel, J, et al. (1993). Uretero-fallopian tube fistula secondary to laparoscopic fulguration of pelvic endometriosis. *J Urol*, 149; 1128-1129.
6. Golan, A, et al. (1984). Fulguration versus resection of experimental endometrial peritoneal implants in the rat. *Aust N Z J Obstet Gynaecol*, 24; 286-288.
7. Redwine, DB (1987). The distribution of endometriosis in the pelvis by age groups and fertility. *Fertil Steril*, 47; 173-175.
8. Sutton, CJ, et al. (1994). Prospective, randomized, double-blind, controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild, and moderate endometriosis. *Ferti Steril*, 62;969-700.
9. Jones, KD, Sutton, C (2003) Patient satisfaction and changes in pain scores after ablative laparoscopic surgery for stage III-IV endometriosis and endometriotic cysts. *Fertil Steril*, 79;1086-1090.
10. Posadzka, E, et al. (2015). Treatment efficacy for pain complaints in women with endometriosis of the lesser pelvis after laparoscopic electroablation vs CO<sub>2</sub> laser ablation. *Lasers Med Sci*, 30;147-152.
11. Healey, M, et al. (2014). To excise or ablate endometriosis? A prospective randomized double-blinded trial after 5-year follow-up. *J Minim Invasive Gynecol*, 21;999-1004.

12. Healey, M, et al. (2010). Surgical treatment of endometriosis: a prospective randomized double-blinded trial comparing excision and ablation. *Fertil Steril*, 94;2536-2540.
13. Wright, J, et al. (2005). A randomized trial of excision versus ablation for mild endometriosis. *Fertil Steril*, 83; 1830-1836.
14. Taylor, E, Williams, C (2010). Surgical treatment of endometriosis: location and patterns of disease at reoperation. *Fertil Steril*, 93;57-61.
15. Fritzer, N, et al. (2012). Effects of surgical excision of endometriosis regarding quality of life and psychological well-being: a review. *Womens Health (Lond Engl)*, 8;427-435.
16. Redwine, DB (1991). Conservative laparoscopic excision of endometriosis by sharp dissection: life table analysis of reoperation and persistent or recurrent disease. *Fertil Steril*, 56;628-634.
17. Fritzer, N, et al. (2014). Dyspareunia and quality of sex life after surgical excision of endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol*, 173;1-6.
18. Roman, JD (2010). Surgical treatment of endometriosis in private practice: cohort study with mean follow-up of 3 years. *J Minim Invasive Gynecol*, 17;42-46.
19. Yeung, P Jr, et al. (2013). A pilot feasibility multicenter study of patients after excision of endometriosis. *JSLG*, 17;88-94.
20. Davis, GD, Brooks, RA (1988). Excision of pelvic endometriosis with the carbon dioxide laser laparoscope. *Obstet Gynecol*, 72;816-819.
21. Abbott, J, et al. (2004). Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertil Steril*, 82;878-884.
22. Redwine, DB (2004). *Surgical Management of Endometriosis*. Martin Dunitz, Taylor & Francis Group: New York, NY.
23. Brouwer, R, Woods, RJ (2007). Rectal endometriosis: results of radical excision and review of published work. *ANZ J Surg*, 77;562-571.
24. Mu, D, et al. (2014). Diagnosis and treatment of ureteral endometriosis: study of 23 cases. *Urol J*, 6;1806-1812.
25. Chiantera, V, et al. (2016). Laparoscopic en bloc right diaphragmatic peritonectomy for diaphragmatic endometriosis according to the Sugarbaker Technique. *J Minim Invasive Gynecol*, 23;198-205.