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Ferromagnetic Dissection in a Rat Glioma Model

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Abstract

Background: We compared cutting and coagulation of a novel ferromagnetic tool (FMwand) with modalities currently used in the clinical setting. Methods: 24 F344 rats with 9L gliosarcoma flank tumours were randomized into 2 groups (n = 12): 1) Five parallel incisions were made into the tumor of each rat using monopolar electrosurgery (MES) cut mode, MES coagulation (coag) mode, FMwand, carbon dioxide (CO_2) laser and cold scalpel. 2) Two parallel incisions were made comparing the MES and the FMwand, both with resecting loop tips. The study was then repeated by a second surgeon. The surgeons applied a grading scale (1 = worst, 5 = best) based on their observations. Results: Average scores for FMwand were superior in ease of tissue dissection (3.58), distortion upon tissues (3.67), and smoke production (2.87). CO_2 laser led in effectiveness of hemostasis (4.32). MES cut mode had the highest scores for ease of cleaning of tip (3.17) and speed of dissection (3.92). The FMwand loop device led in all attributes except for ease of cleaning. Conclusions: The FMwand outperformed CO_2 laser significantly in ease and speed. It was superior compared to MES cut mode for hemostasis and superior compared to coag mode in ease and speed, distortion upon tissues and smoke production. The FMwand loop was significantly better compared to MES loop for hemostasis, distortion, ease and speed. The FMwand was shown to be safe and effective for hemostatic soft tissue cutting and coagulation.

Keywords

CO_2 Laser, Ferromagnetic, FMwand, Glioma, Monopolar

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1. Introduction

The use of electrosurgical devices is widespread in the neurosurgical suite and dates back to the beginning of the 20th century [1]. There are several available energy modalities, each with associated benefits, limitations and risks. These different modalities include traditional monopolar/bipolar, laser, ultrasonic and resistive heating. All of these modalities operate by heating the target tissue in some way. Traditional electrosurgical devices pass low to medium radio frequency (RF) current through the tissue, using the natural resistance of the tissue to create heat [2]. Lasers use focused, coherent light [3], and ultrasonic devices use mechanical vibration to create frictional heat [4] [5]. Other devices use the resistive properties of the materials in the device in conjunction with electrical current to create heat, and then transfer that heat to the target tissue through direct contact.

From a practical perspective, an ideal electrosurgical modality should be able to cut easily and quickly with minimal distortion of the target tissue, to simultaneously stop bleeding in the incisional plane, and do so with minimal smoke production. Additionally, the ability to keep the device clean during a typical surgical procedure is a desirable feature. These traits will be more or less available in different electrosurgical modalities due to the technological and physical limitations inherently found in each.

As an example, typical non-contact laser-based electrosurgical devices do not require any cleaning nor do they cause any tissue distortion, as they do not come in contact with the target tissue during use. This modality should clearly excel in these areas when compared with other electrosurgical tools. Another difference that should be seen in such a comparison is the relative inability of monopolar in cut mode to coagulate, requiring an alternative mode for good hemostasis.

A novel energy modality has recently been introduced with the FMwand (Domain Surgical, Inc. Salt Lake City, Utah, USA) that involves the use of ferromagnetic induction to quickly heat the surgical tip of a handpiece, and transfer that heat to the tissue by direct contact for the purpose of incising soft tissue and simultaneously coagulating in the incisional plane. The FMwand has been FDA cleared for clinical use, and is currently utilized in the United States. The clinical procedures with the ferromagnetic device include surgical treatments of Chiari malformation with syrinx, intraspinal tumors, lumbar disc prolapse, intracranial meningioma and recurrent glioblastoma (University of Texas Medical Branch at Galveston, UTMB, 2013). The device aims to provide unique benefits to the user and the patient that may not be available in other modalities.

MacDonald *et al.* compared the FMwand to monopolar electrocautery and a pulsed radiofrequency device (PlasmaBlade, PEAK Surgical, Inc., Palo Alto, CA, USA) on rabbit liver. The study showed that both newer devices (FMwand, Plasma Device) had significant superior surgical tissue handling characteristics [6]. Bowers *et al.* had similar results with experiments on rabbit muscle comparing the FMwand with monopolar electrocautery showing a significantly less tissue drag with FMwand [7]. A recent controlled and systematic evaluation was done to show that the ferromagnetic device does not cause electromagnetic interference with cardiovascular implantable electronic devices (CIEDs) [8].

This study is designed to explore the strengths as well as the limitations of this new device and to compare it to standard dissection/cauterizing modalities (CO_2 laser and monopolar electrosurgery) in a rat glioma model.

2. Materials and Methods

Animals were housed and treated in accordance with the policies and principles of laboratory care of the Johns Hopkins University School of Medicine Animal Care and Use Committee. The experimental protocol was approved by the Animal Care and Use Committee of the Johns Hopkins University and met all federal guidelines. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. Rats were housed in standard facilities and given free access to Baltimore City water and rat chow.

2.1. Flank Tumor Model

The 9L rodent glioma model is a well-established model for glioma and gliosarcoma research [9]-[12]. The 9L tumor grows in a circumscribed manner and is both aggressive in its growth and dependable in its growth characteristics [10]. The 9L gliosarcoma (a gift from the UCSF Tumor Bank, San Francisco, CA) was maintained as a solid subcutaneous tumor in the flanks of female Fisher 344 rats weighing 125 - 150 g (Harlan Laboratories, Indianapolis, IN). For flank tumor implantation, rats were anesthetized with an intraperitoneal injection containing ketamine hydrochloride 25 mg/ml (Butler Schein Animal, Maryland, USA), xylazine 2.5 mg/ml (Butler Schein Animal, Maryland, USA) and the flanks were shaved and prepared with 70% ethyl alcohol and povidone-iodine solution (Medline Industries, Inc,. Illinois, USA). Under sterile conditions, the tumor was excised and cut into fragments measuring approximately 2 mm^3. The flanks of the experimental animals were similarly prepared for the implantation of the tumor. After a subcutaneous pocket was made on the flank of the experimental animals, the tumor piece was placed inside and the incision was closed with surgical staples. The animals were allowed to recover before being returned to their cages.

2.2. Surgical Devices

The following devices were used in group 1 for linear incisions into the tumor: A monopolar electrosurgery (MES) unit operating at 500 kHz (Valleylab Force 2, Tyco Healthcare Group LP, Boulder, Colorado, USA) performed incisions in "cut(ting)" and "coag(ulation)" mode. A continuous wave CO_2-laser unit (OmniGuide, Cambridge, Massachusetts, USA) and a ferromagnetic electrosurgical unit (FMwand, Domain Surgical Inc., Salt Lake City, Utah, USA) operating at 40.68 MHz were used. A steel scalpel No. 10 blade (Bard Parker, Butler Schein Animal Health, Maryland, USA) was used to create the incisions as control.

In group 2, handpiece dissection tips were removed and debulkment loops were installed on the MES unit and the FMwand unit in order to compare loop debulkment performance in these devices.

2.3. Study Design

F344 rats were divided into two groups of 24 animals each after they had received a flank implantation of a 9L tumor piece 18 days before. In each group, one half of the rats (n = 12) were treated by surgeon 1 (K.C.) and the other half by surgeon 2 (M.G.) (**Figure 1**). The tumor sites were shaved and prepped. In group 1 (n = 24), a skin marker was used to draw five parallel lines onto the tumor of each animal (2 cm length, separated by 1 cm). The skin was incised along the line and incisions into the tumor (depth 1 cm) were made using the 5 investigated instruments (CO_2-laser, MES cut mode, MES coag mode, FMwand and cold scalpel). These cuts were made in a randomized sequence. In group 2 (n = 24), the skin was dissected and a retractor was placed to expose the tumor. Two loop debulkments (2 cm length; 1 cm depth) were made, one with MES loop and one with FMwand loop). The time it took for each instrument was independently recorded by an observer for each cut and debulkment.

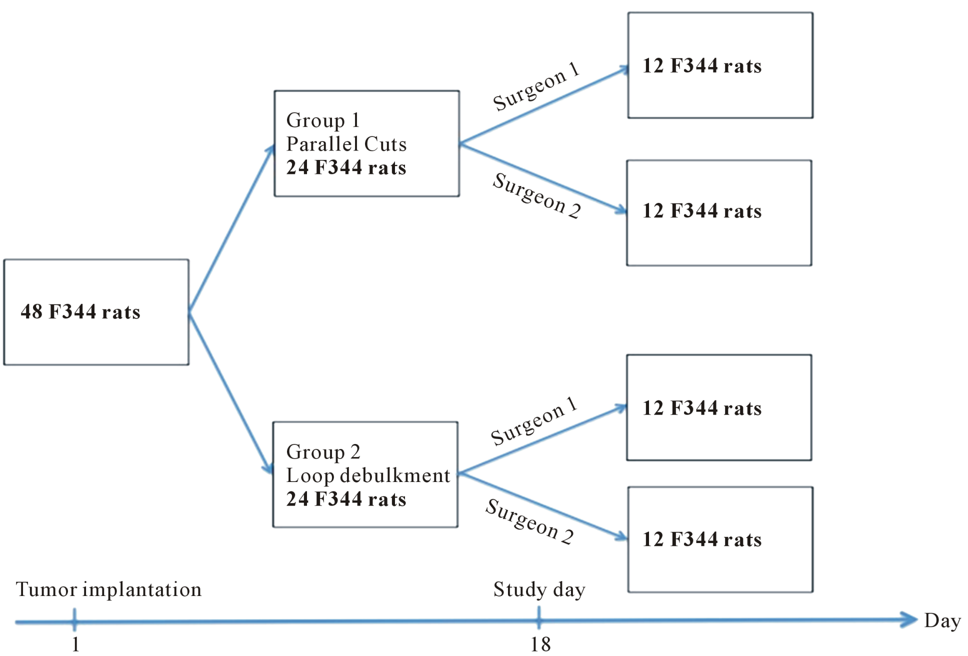

Figure 1. The flow chart shows the study design and its timeline with 9L flank tumor implantation on day 1 and the division of the rats into Groups 1 and 2 on the day of experiments on day 18.

2.4. Surgeons

Two medical doctors in their fifth-year of neurosurgical residencies (M.G, K.C.) carried out the experiments without being informed about the details of the experiment in advance. On the morning of the experiment, the surgeons were shown an instructive video demonstrating how to perform standardized cuts and loop debulkments.

2.5. Scoring System

A scoring system was devised to record the surgeons' observations. Surgeons scored the different devices in 6 different categories: 1) ease of tissue dissection or debulkment, 2) effectiveness of hemostasis, 3) traction or distortion upon tissues, 4) smoke production, 5) ease of cleaning of the tip and 6) speed of dissection. The score of 1 was given for unacceptable or poor performance, 2 for marginal benefit, adaptable to the surgical need with difficulty, 3 for satisfactory performance, 4 for superior performance, improving the tissue injury effect or pace of surgery and 5 for clearly exceptional. After each rat, the surgeon verbally communicated the scores to an independent recorder.

2.6. Histological Evaluation

Animals were euthanized after the surgery. The flank tumors were removed and the tissue was fixed in 10% neutral-buffered formalin solution, embedded in paraffin, sectioned perpendicular to the surgical cuts and stained with hematoxylin and eosin (H&E) (Thermo Fisher Scientific, USA). Hematoxylin binds to basophilic substances, such DNA/RNA and eosin binds to acidophilic substances, such as proteins in the cytoplasm. Slides were examined by a board certified neuropathologist (C.E., Johns Hopkins University) who was blinded with respect to the order of cuts in each specimen. The specimens were graded for hemorrhage and local tissue damage (LTD) within the tumor xenograft on a scale of 0 to 3 (0—none, 1—mild, 2—moderate, and 3—severe).

2.7. Outcome and Statistical Analysis

Descriptive statistics and hypothesis testing were performed using IBM SPSS Statistics 20. Group differences were analyzed using the Mann-Whitney U-Test. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Observational Scores

The observational scores of both surgeons were averaged and compared. **Table 1** highlights the superior device in each category in group 1. The CO_2 Laser as a noncontact instrument was not considered in the category of traction/distortion and ease of cleaning. Cold blade was only considered for histopathological control. The monopolar in "cut mode" was superior in ease of cleaning and speed of dissection, and showed least smoke production in "coag mode". The CO_2 laser showed best hemostasis. The FMwand was rated best in the categories traction/distortion and ease of dissection. **Table 1** also shows that the FMwand was rated better in almost all categories in group 2, and rated equally for ease of cleaning compared to the MES loop device.

Table 1. The table shows the raw data of the observational average scores of both surgeons of Group 1; the high scores are highlighted.

	MES cut	MES coag	CO_2 Laser	FMwand	MES Loop	FMwand Loop
Ease of Dissection	3.46	2.29	2.95	3.59	2.46	4.37
Hemostasis	2.96	3.88	4.32	4.04	3.5	3.82
Traction/Distortion	3.41	2	-	3.67	2.68	4.14
Smoke	2.63	3.83	2.74	2.88	2.69	3
Ease of Cleaning	3.16	2.79	-	3.09	3.55	3.55
Speed of Dissection	3.92	2.38	1.7	3.67	2.77	4.28

3.2. Statistical Analyses

Comparisons were made between each combination of devices for each category using the Mann-Whitney U-Test to determine statistical significance (**Table 2**).

MES cut outperformed MES coag in every category except hemostasis. CO_2 Laser proved significantly better against MES coag in every category except for speed of dissection. FMwand performed well against MES coag, and was significantly better in the categories of ease of dissection, traction/distortion, speed of dissection ($p < 0.0001$) and smoke production ($p < 0.01$). It also was significantly better than the CO_2 laser in ease of dissection ($p < 0.01$) and speed of dissection ($p < 0.0001$). It also showed superior effectiveness of hemostasis when compared to MES cut mode ($p < 0.0001$).

3.3. Loop Debulkment Scores Analysis

In the comparison of the loop debulking tools, the FMwand loop showed statistically significant results in four of the six categories: hemostasis ($p < 0.05$), ease of dissection, traction/distortion of tissues and speed of dissection ($p < 0.0001$). There was no statistically significant difference between the two devices in the other categories (**Table 3**).

3.4. Histopathological Evaluation

Local tissue damage consisted of cautery and reactive cellular changes extending for varying distances from the wound. Hemorrhage comprised red blood cells filling the wound bed and infiltrating into surrounding tumor tissues. These two parameters were scored in the adjacent cuts made with the various instruments by a neuropathologist masked with respect to the order of cuts. Minimal local tissue damage was detected around cuts made by the MES Cut and FMwand, as compared to the more extensive changes with other devices. Variation in the degree of hemorrhage was least in the MES cut wounds, FMwand achieved comparable results. Comparing the wounds of the loop devices, the MES loop showed slightly less tissue damage, while FMwand caused less hemorrhage. MES and FMwand in cutting mode or loop dissection showed similar performance, both with superior performance as compared to the other devices (**Figure 2**).

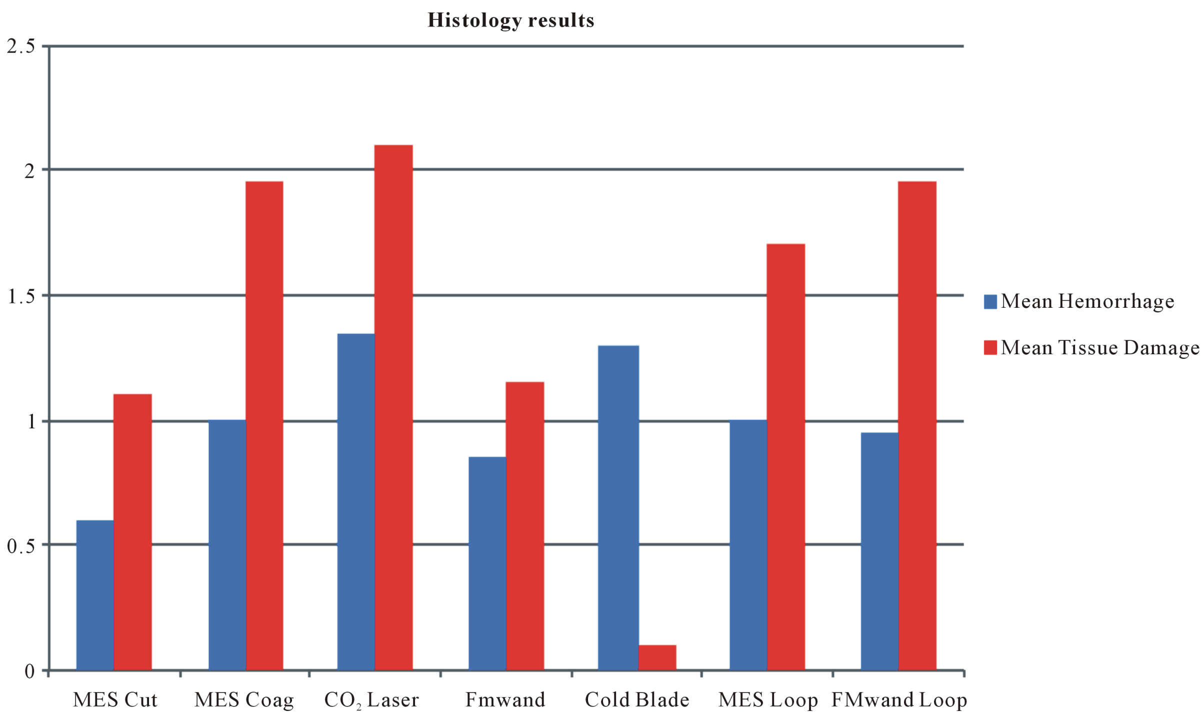

Figure 2. Averages of histological grading of the different devices. The specimens were graded for lateral tissue damage and for hemorrhage with 0 for none, 1 for mild, 2 for moderate, 3 for severe.

Table 2. Each device compared to the other devices using the Mann-Whitney U-Test showing the statistical significant superior device in brackets.

MES cut compared to..	..MES coag	..CO_2 Laser	..FMwand
Ease of dissection	$p < 0.0001$ (MES cut)	$p < 0.05$ (MES cut)	*
Hemostasis	$p < 0.001$ (MES coag)	$p < 0.0001$ (CO_2 laser)	$p < 0.0001$ (FMwand)
Traction/Distortion	$p < 0.0001$ (MES cut)	n/a**	*
Smoke	$p < 0.05$ (MES cut)	*	*
Ease of Cleaning	$p < 0.05$ (MES cut)	n/a	*
Speed of Dissection	$p < 0.0001$ (MES cut)	$p < 0.0001$ (MES cut)	$p < 0.05$ (MES cut)
MES coag compared to..	**..MES Cut**	**..CO_2 Laser**	**..FMwand**
Ease of dissection	$p < 0.0001$ (MES cut)	$p < 0.005$ (CO_2 laser)	$p < 0.0001$ (FMwand)
Hemostasis	$p < 0.001$ (MES coag)	$p < 0.05$ (CO_2 laser)	*
Traction/Distortion	$p < 0.0001$ (MES cut)	n/a	$p < 0.0001$ (FMwand)
Smoke	$p < 0.05$ (MES cut)	$p < 0.005$ (CO_2 laser)	$p < 0.005$ (FMwand)
Ease of Cleaning	$p < 0.05$ (MES cut)	n/a	*
Speed of Dissection	$p < 0.0001$ (MES cut)	$p < 0.005$ (MES coag)	$p < 0.0001$ (FMwand)
CO_2 laser compared to..	**..MES cut**	**..MES coag**	**..FMwand**
Ease of dissection	$p < 0.05$ (MES cut)	$p < 0.005$ (CO_2 laser)	$p < 0.01$ (FMwand)
Hemostasis	$p < 0.0001$ (CO_2 laser)	$p < 0.05$ (CO_2 laser)	*
Traction/Distortion	$p < 0.0001$ (CO_2 laser)	n/a**	$p < 0.0001$ (CO_2 laser)
Smoke	*	$p < 0.005$ (CO_2 laser)	*
Ease of Cleaning	$p < 0.0001$ (CO_2 laser)	n/a	$p < 0.0001$ (CO_2 laser)
Speed of Dissection	$p < 0.0001$ (MES cut)	$p < 0.005$ (MES coag)	$p < 0.0001$ (FMwand)
FMwand compared to..	**..MES cut**	**..MES coag**	**..CO_2 Laser**
Ease of dissection	*	$p < 0.0001$ (FMwand)	$p < 0.01$ (FMwand)
Hemostasis	$p < 0.0001$ (FMwand)	*	*
Traction/Distortion	*	$p < 0.0001$ (FMwand)	n/a**
Smoke	*	$p < 0.005$ (FMwand)	*
Ease of Cleaning	*	*	n/a
Speed of Dissection	$p < 0.05$ (MES cut)	$p < 0.0001$ (FMwand)	$p < 0.0001$ (FMwand)

*no statistical significant difference; **n/a: not applicable.

Table 3. MES loop compared to FMwand loop using the Mann-Whitney U-Test listing the statistical significant superior device.

	MES Loop compared to FMwand Loop
Ease of dissection	FMwand $p < 0.0001$
Hemostasis	FMwand $p < 0.05$
Traction/Distortion	FMwand $p < 0.0001$
Smoke	*
Ease of Cleaning	*
Speed of Dissection	FMwand $p < 0.0001$

*no statistical significant difference.

4. Discussion

The FMwand is FDA cleared, CE Marked and is being used clinically in the United States and Europe. The first human surgeries were performed in December of 2011. At the time of this submission, the FMwand has since been used at over 100 hospitals, by more than 200 surgeons, and in more than 1000 surgeries. The surgical specialties now trialing the FMwand include Neurosurgery, Surgical Oncology, Plastic Surgery, Gynecology, Urology, Cardiothoracic surgery, ENT, General Surgery and Orthopaedic surgery. Surgeons who have used the FMwand in the clinical setting have been especially appreciative of the electrically silent, precise and predictable manner in which the device works. Future randomized clinical studies are needed to examine the merits and demerits of this device in the clinical setting.

This study was designed to explore early surgical impressions of different energy modalities, including the ferromagnetic method and CO_2 laser, alongside the long-established method of standard monopolar electrosurgery and the non-energy method of cold scalpel. A multitude of studies have compared the effects of different instruments on different tissue types [13]-[16]. Studies have been initiated experimentally comparing the new ferromagnetic tool with current standard methods. However, this study is the first to report histological and observational comparisons of LTD produced during incision into rodent tumor by CO_2 laser, MES, FMwand and cold scalpel.

Neither surgeon had previous experience with the new energy modality, but well established working familiarity with RF performance, CO_2 laser and cold scalpel. The approach of incision through skin and into the deep substance of an established flank glioma model provided a variety of tissue types, varying from normal skin and muscular fascia to hypervascular as well as necrotic regions of tumor. The newly introduced surgeons adapted to the characteristics of operation quickly without challenge.

Among the attributes of incisional efficacy, obvious extremes were seen. A cold blade, clearly makes no smoke, but is nonhemostatic, requiring tissue compression or stretch with a retractor to control marginal bleeding. The monopolar cut waveform had little tissue drag, making it efficient for dissection, but hemostasis was poor, again requiring a second step with another instrument or retraction for bleeding control. The monopolar coagulation waveform was highly hemostatic as well as efficient for speed, but obvious charring, deep marginal desiccation, and sparking were seen. CO_2 laser is a noncontact instrument with an invisible beam. Therefore, there is no tissue traction or distortion. Its energy is absorbed very superficially, requiring focused attention at the air-tissue interface. It was hemostatic, but the least effective for speed of incision. Ferromagnetic dissection was modestly less efficient in speed compared to monopolar cut, but showed good hemostasis and no deep thermal injury of desiccation, charring or sparking. It also showed the least tissue marginal distortion comparable to monopolar coag.

Electrosurgery instruments lead to inadvertent damage to nearby anatomical structures through the lateral spread of thermal energy [17]. Large thermal spread of monopolar devices limits their applications onto different tissues [2]. Ferromagnetic and CO_2 laser methods are both thermal, but with markedly diminished “beyond the tip” effects compared to monopolar RF. Ferromagnetic dissection is achieved with a purely thermal effect of heat conduction at the surface of the tip against tissue. CO_2 laser, while dominantly a thermal effect, absorbs entirely into water, leading to similarly minimal absorption beyond the point of beam contact. The extensively studied CO_2 laser has proven to be superior to monopolar electrocautery in minimizing collateral tissue damage [18]. Thus, they are comparable as energy modalities by their very shallow injury margins. While ferromagnetic dissection has minimal traction compared to no traction with CO_2 laser, the tactile contact feedback was also seen as helpful in tissue control. It was comparably more efficient in speed of dissection.

This investigation did not compare ultrasound, a fourth energy modality frequently employed. The study illustrates unique strengths and weaknesses of energy modalities which a surgeon might select for various tissue types, based on location, vascularity, proximity to critical margins of vessels and neural tissue, and need for minimal distortion. As such, the two newer modalities of ferromagnetic and CO_2 laser have especially attractive features for hemostasis, minimal tissue injury, and minimal traction/distortion. However, ferromagnetic was clearly more efficient for dissection speed. A further advantage of the ferromagnetic method is a loop resector configuration for tissue debulkment. The ferromagnetic loop performed superiorly statistically for hemostasis, speed and tissue distortion compared to the monopolar loop.

Each instrument has its potential advantages and disadvantages. Surgeons should test various instruments not only for characteristics of dissection and hemostasis, but also to become familiar with the tensile strength, geometry, weight, shaft angle, and length of the various instruments [19]. Previous studies suggest that different modalities cause varying, distinctive granulation tissue patterns [20]. Further study is required to determine these long-term effects of this new energy modality compared to monopolar RF or CO_2 laser.

5. Conclusion

The histologic and observational findings of this study suggest that FMwand is safe and effective for hemostatic soft-tissue cutting and coagulation. Further investigation including the evaluation of soft-tissue healing is mandatory to determine the long-term efficiency of the novel modality.

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Declaration of Interest

The study was kindly funded by Domain Surgical. However, the data was obtained independently from blinded reviewers. The instruments used in the study were provided for the study by the respective manufacturers (Valleylab, Omniguide, Domain Surgical). The study was independent of the manufacturers of the tested surgical instruments.

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