Title page

Title of the article: Comparison of PEAK PlasmaBlade™ to conventional diathermy in abdominal based free flap breast reconstruction surgery - a single centre double blinded randomised controlled trial.

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Summary

Background: Electrosurgery makes dissection with simultaneous haemostasis possible. The produced heat can cause injury to the surrounding tissue. The PEAK PlasmaBlade™ (PPB) is a new electrosurgery device which may overcome this by having the ability to operate on a lower temperature, therefore reducing collateral thermal damage.

Method: A double blinded, single centre, randomised controlled trial was conducted which included 108 abdominal based free flap breast reconstruction patients who had their flap raise performed using either the PPB (n=56) or conventional diathermy (n=52). Data were collected during their in-patient stay and out-patient appointments. The primary outcome value was the number of days the abdominal drains were required.

Results: Baseline characteristics were similar between the groups, except a significantly lower flap weight in the PPB group. The median number of days the drains were required did not differ significantly (p=0.48; 6.0 days for the diathermy and 5.0 days for PPB). The total drain output (p=0.68), the inflammatory cytokine in the drain fluid (p>0.054) and complications (p>0.24) not differ significantly between the two groups. At the 2-week follow-up appointment there was a trend towards less abdominal seromas on abdominal ultrasound (p=0.09) in the PPB group which were significantly smaller (p=0.04).

Conclusion: The use of the PPB did not result in a significant reduction of drain requirement, total drain output or inflammatory cytokines but did reduce the size of seroma collections at the 2-week follow-up appointment. Therefore, the use of the PEAK PlasmaBlade™ device could reduce early seroma formation after drain removal.

Keywords

Electrosurgery; conventional diathermy; PEAK PlasmaBlade™; abdominal based autologous breast reconstruction; inflammatory cytokines; seroma

Text

Introduction

In woman, breast cancer is with 24.2% the most commonly diagnosed cancer, affecting 2.1 million women each year worldwide [1]. The aim of breast reconstruction is to restore shape and symmetry and is increasingly considered an important component of breast cancer management [2]. Autologous reconstruction is considered the gold standard in breast reconstruction [3] but disadvantages include an operating time of 4-6 hours, donor site morbidity and a recovery period up to three months [4].

A seroma is a collection of non-infected subcutaneous fluid and one of the most frequent donor site complications after autologous abdominal based breast reconstruction [5]. Due to the uncertain pathophysiology there is no consensus on how to reduce its occurrence.

Electrosurgery uses a high-frequency electrical current for tissue dissection and simultaneous haemostasis [6, 7]. The downside of this technique is the collateral thermal damage to the surrounding tissue, which could lead to complications [8-11]. Electrosurgery in abdominoplasties has been linked to seroma formation [11-14]. The initial response to trauma, such as surgery is largely coordinated by endogenous soluble mediators referred to as inflammatory cytokines [15, 16]. A higher degree of tissue injury results in production of higher levels of pro-inflammatory cytokines, which can be measured in wound fluid [8, 17]. Levels of most cytokines are highest 24-hours after the injury [18, 19].

Over recent years alternatives to the conventional “Bovie” diathermy have been developed trying to improve efficiency and reduce collateral tissue damage. One of these devices is the PEAK PlasmaBlade™ (PPB)which can operate on a lower temperature due to very brief pulses of radiofrequency energy [20]. Different experimental studies in both animal and human models comparing the PEAK PlasmaBlade™ and other surgical dissection devices for incisions have shown a reduction in width of zone of thermal injury, reduction in wound inflammation, increased wound strength and reduced scaring in favour of the PEAK

PlasmaBlade™ [20-23]. Some clinical studies comparing the PEAK PlasmaBlade™ to other modalities for tissue dissection show a reduction in total drainage, drain requirement and/ or seroma formation [24-27].

The aim of this study is to compare the PEAK PlasmaBlade™ with the conventional diathermy for the raise of abdominal free flaps in immediate and delayed breast reconstruction patients and compare outcomes such as drain requirement, total drainage, inflammatory markers in drain fluid and complications such as wound healing problems and seroma formation.

Patients and Methods

A single centre, double blinded randomised controlled trial (RCT) adhering to CONSORT guidelines was conducted between November 2016 and May 2018. The study was reviewed and approved by the East of England - Cambridge Central Research Ethics Committee (REC reference: 16/EE/0005, Protocol number: 137680 and IRAS project ID: 192471) and Anglia Ruskin University Faculty Research Ethics Panel. The study participants meeting the in- and exclusion criteria (Table 1) received an information leaflet and a written consent was obtained before enrolment. Randomisation was performed using the online randomisation service of the Trans European Network for Clinical Trials Service (TENALEA). Enrolled patients underwent a 1:1 block randomisation (block size 6). The patients and investigator collecting the data were both blinded for which machine was used. All patients underwent a standardised DIEP or MS-TRAM breast reconstruction performed by one of the two senior authors (MG or VR) with either the conventional diathermy or the PEAK PlasmaBlade™. The standardised maximum power settings for the diathermy were cut 40-Watt, coagulation 40-Watt and for the PEAK PlasmaBlade™ cutting 7 (35-Watt), coagulation 7 (35-Watt). If the bipolar was required for haemostasis it was not used above 15 Watt.

At the end of the procedure each patient received two abdominal 15 French Blake drains connected to a low vacuum wound drainage system (85 kPa/neg 100mmHg). Drains were

removed as per protocol when they produced ≤30mL/24hours, with a maximum of 14 days. Patients would also wear an abdominal binder for six weeks post-operatively.

During their admission patients were seen twice a day to collect data on abdominal drain output (mL), pain by using a numerical rating scale (NRS 0 – 10), morphine consumption (mg), daily mobility using a pedometer (steps) and complications. Drain fluid samples were collected on day 0, 1 and 2 and stored in a -80ºC freezer. For analysis they were transported on dry ice to Myriad RBM, Inc. a clinical laboratory improvement amendments (CLIA) certified biomarker testing laboratory located in Austin, Texas (United States).

After discharge, patients were seen in the out-patient clinic, two and six weeks after surgery where an abdominal ultrasound was performed to identify seroma collections. If a seroma collection was present the length, width and maximum height were measured. The volume (cm^3 = mL) of the identified collection was estimated by using the formula of half an ellipsoid: $\frac{4}{3}\pi\ abc$. Large seromas would only be percutaneously drained if they were causing discomfort to the patient.

The primary outcome for which this RCT was powered, was the amount of days abdominal drains were required. Secondary outcome values were operating time (min), inflammatory markers in drain fluid on day 0,1 and 2, pain scores, total abdominal drain fluid output (mL), mobility and abdominal donor site complications such as wound breakdown, infection and seroma.

Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (SPSS, Inc., Chicago, USA). With data from our pilot study [28] a power calculation for the primary outcome was performed, using the Lehr's formula with a 5% significance level to give a power of 80%. This resulted in a minimal sample size of 53 patients for each group.

To determine if acquired continuous data was normally distributed the Shapiro-Wilk test was applied. If normally distributed the independent samples t-test was used to establish if there was a statistically significant difference between the two groups. If not normally distributed the Mann-Whitney U Test was used. To calculate statistical significance for categorical data the Pearson Chi-Square Test for numbers over 5, if the count was equal to or less than 5 the Fisher's Exact Test was used.

Linear regression was used to identify determinants for the time to drain removal. Logistic regression was used to identify determinants for the presence of seroma at the 2-week and 6-week abdominal ultrasound scan and for the occurrence of complications. Variables that had a significant p-value in the univariate analysis were included in a multivariable analysis.

A value below or equal to 0.05 was considered to be statistically significant.

Results

Baseline characteristics of the study population

During the 19-month recruitment period, 119 patients were recruited and randomised. Eleven patients were excluded from the study following clinically necessary pre- or peri-operative diversion from the protocol, not caused by the surgical instrument used. Resulting in a final study population of 108 patients. Fifty-two patients were randomised to the conventional diathermy and 56 to the PEAK PlasmaBlade™ group. The baseline characteristics of the all-female patient population are shown in Table 2.

Peri-operative data

Data recorded during the operation showed a statistically significant difference (p=0.03) in flap weight between the two groups. All other data were comparable between the two groups (Table 3).

Inflammatory markers

Samples of drain fluid collected on day 0,1 and 2 were analysed to determine the levels of the inflammatory cytokines TNF-alpha, IL-4, IL-6, IL-8, IL-10, IL-18, MIP-1 alpha, MIP-1 beta and MCP-1. There was a trend towards lower values for inflammatory cytokines MIP-1 beta on day 0 (p=0.07), MIP-1 alpha on day 1 (p=0.054) and IL-18 on day 2 (p=0.07) in the PEAK PlasmaBlade™ group, but none reached statistical significance (Table 4).

Abdominal drains

There was no statistically significant difference (p=0.68) between the total volume drained in the conventional diathermy group (342.5 mL (IQR 233.8 – 618.8)) and the PEAK PlasmaBlade™ group (355.0 mL (IQR 228.8 – 532.5)). In the PEAK PlasmaBlade™ group, the drains were required for 5 (IQR 5.0 – 8.0) days, compared to 6 (IQR 5.0 – 8.8) days in the conventional diathermy group, not reaching statistical significance (p=0.48) (Table 5).

In diagram 1 are two histograms showing the distribution of the amount of days the drains were required for the two different study groups.

Diagram 2 shows the Kaplan-Meier curve. All patients were included, but the 19 patients who had their drains remove too early (draining more than 30 ml/ 24hours) were censored. There was no statistically significant difference between the two groups using the Log Rank test, with a p-value of 0.42.

Pain scores

The only statistically significant result was the median pain score post-operatively, in recovery (day 0). The PEAK PlasmaBlade™ group had a statistically significant (p=0.02) higher median pain score of 4 (IQR 1.0 – 6.0), compared to the conventional diathermy group with a pain score of 2 (IQR 1.0 – 5.0).

Complications

Table 6 shows complications were evenly distributed between the two groups, not showing any statistically significant differences.

Seroma on abdominal ultrasound scan

There was a trend towards less seromas in the PEAK PlasmaBlade™ at the 2-week follow-up appointment, almost reaching statistical significance (70.6% vs 54.5%, p=0.09). At the 2-week follow-up appointment the total seroma size (cm^3) was significantly smaller in the PEAK PlasmaBlade™ group compared to the normal diathermy group (62.8cm^3 (IQR 88.0) vs 45.6cm^3 (IQR 81.2), p=0.04). At the 6-week follow-up appointment there were no statistically significant differences in presence and size of seromas between the two groups (Table 7).

Cox proportional hazards model for days drains were required

Comparing the machines used, the hazards ratio for the number of days drains were required was 1.16 (95% confidence interval 0.76 - 1.76; table 8), which did not reach statistical significance (p=0.50). Other factors such as age, BMI, flap weight, consultant, procedure and adjuvant therapies were analysed for their association with time to drain removal. BMI and flap weight were statistically significantly inversely associated with time to drain removal (Table 8).

Three multivariable analyses were conducted. In the first analysis, machine use was adjusted for BMI. In the second analysis, machine use was adjusted for flap weight. In the third multivariable analysis, machine use was adjusted for both BMI and flap weight (Table 9).

After correction for predictors delaying drain removal, the type of machine used was not significantly associated with the length of drain requirement.

Logistic regression for seroma presence on 2- and 6-week ultrasound

A logistic regression was performed for the presence of seroma on ultrasound at 2- and 6-week follow-up appointments, to review the influence of different parameters. The odds ratio of 0.5 (95% confidence interval 0.22 – 1.12) for the machine's association with seroma incidence at the 2-week ultrasound almost reached statistical significance (p=0.09) (Table 10). At the 6-week ultrasound the odds ratio of 0.79 (95% confidence interval 0.32 – 1.95) for the machine's association with seroma incidence did not reach statistical significance (p=0.62) (Table 11).

Univariable logistic regression for the 2-week seroma presence did not show any significant parameters, therefore age and consultant both with a p value <0.10 were used in the multivariable logistic regression (Table 10).

Univariable logistic regression for the 6-week seroma presence did show a significant odds ratio for age (p=0.005) and consultant (p=0.03). Both values were used in the multivariable logistic regression (Table 11).

After multivariable logistic regression adjusting for age and consultant, the type of machine used was not significantly associated with the presence of a seroma collection at the 2-week ultrasound (Table 12). The same was shown in the multivariable logistic regression for the 6-week ultrasound (Table 13).

Logistic regression for complications

A logistic regression was performed for all the experienced complications. The number of complications experienced by each patient ranged from 0 to 3. Results from univariable analysis are displayed in Table 14.

A higher BMI was associated with a higher number of complications, reaching statistical significance (p=0.045).

Two multivariable analyses were conducted. The first analysis adjusted for BMI only, as this was the only statistically significant predictor for complications in the univariate analysis. The second analysis adjusted for all variables with a p-value smaller than 0.2 (BMI and flap weight, Table 15). After correction for predictors for complications, the type of machine used was not associated with a higher number of complications.

Discussion

Since its introduction in the early 1900s, electrosurgery has become an important tool in surgical practice [29] as it enables surgeons to cut and perform haemostasis simultaneously. Experimental studies in animals raised the concern electrosurgery could lead to poor wound healing and an increased risk of complications such as surgical site infection, however clinical trials do not seem to support this [29-32]. A seroma is an accumulation of non-infectious fluid and is one of the most common abdominal donor site complications after abdominal based free-flap breast reconstruction. The origin is not well understood, but is most likely multifactorial, with electrosurgery postulated to be one of the factors worsening the inflammatory response [5, 11, 14, 33, 34]. A seroma can cause discomfort, wound breakdown, infection and if chronic, can turn into a pseudocyst [5, 9, 34].

The PEAK PlasmaBlade™ is a new electrosurgical device (Medtronic Advanced Energy, LLC., Portsmouth, New Hampshire) which uses very brief pulses (40μsec) of radio frequency energy to create electrical plasma along the edge of a thin (12.5μm) 99.5% insulated electrode, creating a cutting edge with simultaneous homeostatic properties [20, 35]. Depending on the settings this technology uses less total energy and can operate at significantly lower temperatures than traditional electrosurgical devices which leads to less collateral thermal damage [20]. Experimental studies have shown skin incisions with the PEAK PlasmaBlade™ used in a low cut mode setting (6 Watt) have a wound-healing profile comparable to that of scalpel incisions and superior to those of conventional electrosurgical incisions with respect to zone of thermal injury, inflammation, wound strength and scar formation [20, 22, 35, 36]. In

breast surgery, Dogan et al. [24] published a statistically significant difference between drain output and drainage duration in mastectomies favouring the use of the PEAK PlasmaBlade™ (n=24) over conventional electrocautery (n=22).

Our RCT has been unable to show a statistically significant reduction in abdominal drain requirement or total drain output after performing the abdominal flap raise with the PEAK PlasmaBlade™. A possible explanation for the inability to find a significant difference between the two electrosurgery devices is their similarity at higher power settings in both cut and coagulation mode, resulting in comparable amounts of collateral thermal damage. The favorable wound healing profile and reduced zone of thermal injury shown in the experimental studies was at low energy settings (3 = 6-Watt) in the cut mode. Clinical studies published in recent years show inconsistent results for both drain requirement and total drain output which could be due to poor study designs and other confounding factors [25-27, 37].

The operative time for the PEAK PlasmaBlade™ (120min IQR 93.5 – 154.5), did not differ significantly from the conventional diathermy (129min IQR 90 – 159.3). This shows the use of the new technology of the PEAK PlasmaBlade™ only requires a short learning curve and is as effective for dissection and haemostasis as the conventional diathermy.

In the immediate post-operative period in recovery pain was significantly higher in the PEAK PlasmaBlade™ group. A possible explanation for this could be correlated to the significantly lower flap weight in the PPB group resulting in a tighter more painful abdominal closure. Axillary lymph node clearance was more common in the PEAK PlasmaBlade™ group (32.1% vs 21.2%), but this did not reach statistical significance. Possibly the difference in pain score is based on interpatient variability as pain remains a subjective matter.

Ozdogan et al. [8] and Yilmaz et al. [17] showed a significant difference in levels of TNF-alpha and IL-6 in 24-hour post mastectomy drain fluid, between knife and electrosurgical dissection.

We found a trend towards lower values for inflammatory cytokines MIP-1 beta on day 0 (p=0.07), MIP-1 alpha on day 1 (p=0.054) and IL-18 on day 2 (p=0.07) in the PEAK PlasmaBlade™ group, but none reach statistical significance. This finding supports the hypothesis that if the PEAK PlasmaBlade™ is used at higher energy settings in both the cut and coagulation mode its' operating temperature will rise resulting in more collateral tissue damage comparable to that of the conventional diathermy.

In our study seromas were very common (61% of patients), but only required intervention in 5.6% of cases. At the two-week follow-up appointment seromas were more common in the conventional diathermy group, almost reaching statistically significance (p=0.09). Seroma collections were statistical significantly smaller (p=0.04) in the PEAK PlasmaBlade™ group. These differences had resolved at the 6-week follow-up appointment, where in both groups the seromas had significantly reduced in number and size by spontaneous re-absorption.

Limitation of study

Despite randomisation, the flap weight was significantly (p=0.03) higher in the conventional diathermy group, making it a confounder in this study. Multivariable regression was performed to correct for this difference.

Conclusion

Experimental studies on the use of the PEAK PlasmaBlade™ have showed very promising results, with regards to wound healing profiles and reduction in collateral thermal injury. Though clinical studies so far have mostly been unable to reveal significant improvement in post-operative recovery and a reduction in complications, possibly due small numbers and bias following poor design.

This conducted large double blinded randomised controlled trial including 108 abdominal free-flap breast reconstruction patients has been unable to show a statistically significant difference

in drain requirement, total drainage or complications between patients operated with the conventional diathermy and the PEAK PlasmaBlade™ using the cut 7 and coagulation 7 settings. Inflammatory marker levels were similar between the two study groups, suggesting comparable inflammatory responses. There was a trend towards less seromas at the 2-week follow-up appointment, which were significantly smaller in the PEAK PlasmaBlade™ group. Therefore, the PEAK PlasmaBlade™ device could reduce early seroma formation after drain removal, which can decrease seroma associated complication such as wound healing problems and infection. Despite the high incidence of seromas on ultrasound after abdominal based autologous breast reconstruction, intervention was rarely required in either of the two groups.

These results can also be considered for other procedures resulting in large (donor site) wounds such as latissimus dorsi breast reconstruction, cosmetic abdominoplasties and abdominal wall reconstructions.

For future high-quality clinical trials, it would be interesting to evaluate the potential benefit of the PEAK PlasmaBlade™ in a similar model but at lower power settings.

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Tables

Table 1. In-/exclusion criteria

Inclusion Criteria	Exclusion criteria
Adult (18-80 years) able to consent	Children (<18yrs) Adults older than 80 years
Unilateral immediate or delayed DIEP/ MS-TRAM breast reconstruction	Bilateral or bi-pedicled DIEP/ MS-TRAM breast reconstructions
BMI >20	BMI < 20
	Diabetic
	Immuno-suppression
	Ischaemic heart disease
	Clotting disorders
	On steroid medication
	Pregnancy
	Active smoking

Table 2. Patient characteristics of the two study groups

Characteristic	Conventional diathermy (n=52)	PEAK PlasmaBlade™ (n=56)	p-value
Age (yr) †	52.5 (45.0 – 62.8)	52 (44.0 – 60.0)	0.44
Height (cm) †	161 (154.3 – 168.6))	163 (158.0 – 169.0)	0.32
Weight (kg) *	76.8 ± 12.1	75.0 ± 13.5	0.44
Body mass index†	28.6 (26.0 – 32.6)	27.7 (24.7 – 31.38)	0.14
Consultant (MG/VR)	17/35	16/40	0.68∂
Procedure (DIEP/MS-TRAM)	50/2	52/4	0.68Δ
Timing (immediate/delayed)	39/13	43/13	0.83∂
Axillary clearance	21.2%	32.1%	0.20∂
SLNB	11.5%	10.7%	0.90∂
Procedure ipsilateral breast	34.6%	28.6%	0.50∂
Pre-op radiotherapy	28.8%	28.6%	1.00∂
Neo-adjuvant chemotherapy	21.2%	25%	0.66∂
Hormone Therapy	28.8%	26.8%	0.83∂

* Mean ± SD; Independent samples t-test
† Median (IQR); Mann-Whitney U test
∂ Pearson Chi-Square test
Δ Fisher's Exact test
SLNB = sentinel lymph node biopsy
SD = Standard Deviation; IQR = Interquartile Range

Table 3. Peri-operative data

Characteristic	Conventional diathermy	PEAK PlasmaBlade™	p-value
Time flap raise (min) †	129.0 (90.0 – 159.3)	120.0 (93.5- 154.5)	0.80
Number of perforators†	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	0.47
Number of vessel clip packs†	12.0 (9.0 – 25.0)	12.0 (9.0 – 14.0)	0.63
Flap weight (g) †	958.5 (759.0 – 1239.0)	833.0 (575.0 – 1031.0)	0.03
Amount of IV fluid given (L) †	2.0 (1.8 – 2.5)	2.0 (2.0 – 2.5)	0.41

†Median (IQR); Mann-Whitney U test
IV = Intravenous; min = minutes; mg = milligram; L = litre

Table 4. Inflammatory Cytokines in drain fluid on day 0,1 and 2

		Conventional diathermy (n=52)	PEAK PlasmaBlade™ (n=56)	p-value
Day 0	**TNF-alpha**†	62.0 (20.0 – 62.0)	62.0 (20.0 – 62.0)	0.40^
	IL-4†	45.0 (26.0 – 45.0)	45.0 (26.0 – 45.0)	0.85^
	IL-6†	28150.0 (8777.5 – 55875.0)	26600.0 (7552.5 – 46200.0)	0.40^
	IL-8†	8450.0 (23253.0)	9695.0 (19828.0)	0.90^
	IL-10†	56.5 (36.5 – 93.0)	49.5 (35.3 – 67.5)	0.31*
	IL-18†	444.5 (353.8 – 630.8)	447.0 (325.5 – 610.0)	0.77*
	MIP-1 alpha†	83.5 (57.3 – 139.5)	77.5 (55.8 – 125.8)	0.50^
	MIP-1 beta†	1500.0 (961.5 – 2200.0)	1215.0 (706.0 – 1705.0)	0.07^
	MCP-1†	20550.0 (9952.5 – 48175.0)	23050.0 (8447.5 – 42400.0)	0.70^
Day 1	**TNF-alpha**†	62.0 (22.0 – 62.0)	62.0 (22.0 – 62.0)	0.91^
	IL-4†	43.5 (26.0 -45.0)	45.0 (26.0 – 45.0)	0.69^
	IL-6†	36150.0 (23175.0 – 47325.0)	38650.0 (21450.0 – 48025.0)	0.90^

	IL-8†	20600.0 (9795.0 – 52175.0)	18900.0 (9012.5 – 31075.0)	0.53^
	IL-10†	127.0 (86.8 – 170.3)	119.0 (88.5 – 144.5)	0.60*
	IL-18†	443.5 (290.5 – 577.8)	362.0 (258.0 – 523.5)	0.30*
	MIP-1 alpha†	84.0 (58.0 – 151.5)	68.5 (50.0 – 103.3)	0.054^
	MIP-1 beta†	2210.0 (1197.5 – 3222.5)	1540.0 (895.0 – 2665.0)	0.20^
	MCP-1†	33850.0 (21200.0 – 53375.0)	31100.0 (20525.0 – 53850.0)	0.86^
Day 2	**TNF-alpha†**	62.0 (29.0 – 62.0)	62.0 (25.3 – 62.0)	0.48^
	IL-4†	45.0 (19.0)	45.0 (19.0)	0.70^
	IL-6†	19000.0 (9895.0 – 26850.0)	13650.0 (10067.5 – 18700.0)	0.10^
	IL-8†	22950.0 (10425.0 – 50725.0)	17350.0 (10200.0 – 30075.0)	0.14^
Day 2	**IL-10†**	115.5 (77.0 – 155.0)	104.5 (86.3 – 138.8)	0.96*
	IL-18†	382.5 (243.0 – 517.3)	300.5 (222.8 - 431.5)	0.054*
	MIP-1 alpha†	116.0 (80.0 – 181.8)	97.5 (79.0 – 155.0)	0.19^
	MIP-1 beta†	2160.0 (1515.0 – 3487.5)	1920.0 (1390.0 – 3047.5)	0.31^
	MCP-1†	35350.0 (22200.0 – 49250.0)	36500.0 (22700.0 – 55650.0)	0.96^

† Median (IQR)
* Independent sample t-test for normally distributed data after ^{10}log transformation
^ Mann-Whitney U test for not normally distributed data after ^{10}log transformation

Table 5. Abdominal drains	**Conventional diathermy (n=52)**	**PEAK PlasmaBlade™ (n=56)**	**p-value**
Volume drain fluid (mL) †	342.5 (233.8 – 618.8)	355.0 (228.8 – 532.5)	0.68
Number of days drains required all patients†	6.0 (5.0 – 8.8)	5.0 (5.0 – 8.5)	0.48

† Mann-Whitney U test; Median (IQR)

Table 6. Complications				
Intervention		**Conventional diathermy (n=52)**	**PEAK PlasmaBlade™ (n=56)**	**p-value**
Free flap problem	Theatre	6	3	0.31[Δ]
Abdominal haematoma	Conservative	1	0	0.23[Δ]
	Theatre	1	0	
Abdominal seroma causing discomfort	Needle aspiration	2	2	1.00[Δ]
Abdominal seroma causing wound breakdown	Theatre	1	1	1.00[Δ]
Abdominal wound infection	Oral antibiotics	0	2	0.50[Δ]
Partial abdominal wound breakdown	Wound dressings	4	5	1.00[Δ]
Total amount of complications		15	13	0.58[∂]
[Δ] Fisher's Exact test, [∂] Pearson Chi-Square test				

Table 7. Seroma on abdominal ultrasound scan		**Conventional diathermy**	**PEAK PlasmaBlade™**	**p-value**
2 weeks	**Presence of seroma** [†]	70.6%	54.5%	0.09
	Largest seroma collection (cm^3) [†]	51.5 (22.0 – 95.7)	41.8 (15.0 – 73.4)	0.03
	Total seroma collections (cm^3) [†]	62.8 (22.0 – 110.0)	45.6 (16.8 – 98.0)	0.04
6 weeks	**Presence of seroma** [†]	26.0%	23.2%	0.78
	Largest seroma collection (cm^3) [†]	16.1 (11.6 –115.8)	19.3 (12.9 – 37.6)	0.98
	Total seroma collections (cm^3) [†]	16.5 (11.6 – 115.8)	22.1 (12.9 – 43.4)	0.94
[†]Median (IQR); Mann-Whitney U Test				

Table 8. Univariable Cox regression analysis for drain requirement

	Hazard Ratio	Confidence interval	p-value
Machine (Ref group: diathermy)	1.16	0.76 – 1.76	0.50◊
Age (per 5 years increment)	0.94	0.86 – 1.03	0.21◊
BMI (per 5kg/m^2 increment)	0.78	0.62 – 0.99	0.04◊
Flap weight (per 100g increment)	0.94	0.89 – 0.99	0.03◊
Consultant (Ref group: VR)	0.86	0.53 – 1.40	0.55◊
Procedure (Ref group: DIEP)	1.69	0.73 – 3.90	0.22◊
Radiotherapy (Ref group: no radiotherapy)	0.99	0.62 – 1.58	0.97◊
Neo-adjuvant chemotherapy (Ref group: no chemotherapy)	1.03	0.63 – 1.68	0.92◊
Hormonal therapy (Ref group: no hormonal therapy)	0.98	0.63 – 1.56	0.95◊

◊ Cox Model

Table 9. Multivariable Cox regression analysis

	Multivariable 1	Multivariable 2	Multivariable 3
Machine (Ref group: diathermy)	1.15* (0.76 – 1.75)† p = 0.50◊	1.06* (0.69 – 1.62)† p = 0.79◊	1.08 (0.71 – 1.65) p = 0.72◊

*hazard ratio (HR); †95.0% confidence interval (CI); ◊p-value Cox model
Multivariable 1: only adjusted for BMI (p=0.04)
Multivariable 2: only adjusted for flap weight (p=0.03)
Multivariable 3: adjusted for BMI and flap weight

Table 10. Univariable logistic regression for seroma presence on ultrasound at 2 weeks			
	Odds Ratio	**Confidence interval**	**p-value**
Machine (Ref group: diathermy)	0.50	0.22 – 1.12	0.09◊
Age (per 5-year increment)	1.22	0.999 – 1.50	0.051◊
BMI (per 5kg/m^2 increment)	1.26	0.80 – 1.99	0.32◊
Flap weight (per 100g increment)	1.08	0.97 – 1.21	0.16◊
Consultant (Ref group: VR)	0.44	0.19 – 1.04	0.06◊
Procedure (Ref group: DIEP)	0.59	0.11 – 3.06	0.53◊
Radiotherapy (Ref group: no radiotherapy)	1.15	0.48 – 2.74	0.76◊
Neo-adjuvant chemotherapy (Ref group: no chemotherapy)	0.88	0.35 – 2.21	0.79◊
Hormone therapy (Ref group: no hormonal therapy)	0.72	0.30 – 1.71	0.46◊
◊ Logistic regression model			

Table 11. Univariable logistic regression for seroma presence on ultrasound at 6 weeks			
	Odds Ratio	**Confidence interval**	**p-value**
Machine (Ref group: diathermy)	0.79	0.32 – 1.95	0.62◊
Age (per 5-year increment)	1.41	1.11 – 1.79	0.005◊
BMI (per 5kg/m^2 increment)	1.17	0.72 – 1.90	0.52◊
Flap weight (per 100g increment)	1.07	0.95 – 1.21	0.24◊
Consultant (Ref group: VR)	0.24	0.07 – 0.87	0.03◊
Procedure (Ref group: DIEP)	3.5	0.66 – 18.57	0.14◊
Radiotherapy (Ref group: no radiotherapy)	0.74	0.26 – 2.07	0.56◊
Neo-adjuvant chemotherapy (Ref group: no chemotherapy)	0.80	0.27 – 2.43	0.70◊
Hormone therapy (Ref group: no hormonal therapy)	1.03	0.38 – 2.79	0.96◊
◊ Logistic regression model			

Table 12. Multivariable logistic regression for seroma presence on USS at 2 weeks

	Multivariable 1	Multivariable 2	Multivariable 3
Machine (Ref group: diathermy)	0.53* (0.23 – 1.20)† p = 0.13◊	0.47* (0.21 – 1.07)† p = 0.07◊	0.49* (0.21 – 1.13)† p = 0.09◊

*odds ratio (OR); †95.0% confidence interval (CI); ◊Logistic regression model
Multivariable 1: only adjusted for age (p=0.051)
Multivariable 2: only adjusted for consultant (p=0.06)
Multivariable 3: adjusted for both age and consultant

Table 13. Multivariable logistic regression for seroma presence on USS at 6 weeks

	Multivariable 1	Multivariable 2	Multivariable 3
Machine (Ref group: diathermy)	0.88* (0.34 – 2.25)† p = 0.79◊	0.76* (0.30 – 1.91)† p = 0.56◊	0.86* (0.33 – 2.26)† p = 0.76◊

*odds ratio (OR); †95.0% confidence interval (CI); ◊Logistic regression model
Multivariable 1: only adjusted for age (p=0.005)
Multivariable 2: only adjusted for consultant (p=0.03)
Multivariable 3: adjusted for both age and consultant

Table 14. Univariable logistic regression for complications

	Odds Ratio	Confidence interval	p-value
Machine (Ref group: diathermy)	0.73	0.29 – 1.87	0.52◊
Age (per 5 years increment)	1.10	0.88 – 1.37	0.42◊
BMI (per 5kg/m^2 increment)	1.74	1.01 – 2.98	0.045◊
Flap weight (per 100g increment)	1.11	0.98 – 1.26	0.09◊
Consultant (Ref group: VR)	0.56	0.21 – 1.46	0.24◊
Procedure (Ref group: DIEP)	1.85	0.33 – 10.37	0.48◊
Radiotherapy (Ref group: no radiotherapy)	0.84	0.31 – 2.30	0.73◊
Neo-adjuvant chemotherapy (Ref group: no chemotherapy)	2.24	0.61 – 8.29	0.23◊
Hormonal therapy (Ref group: no hormonal therapy)	0.84	0.31 – 2.31	0.74◊

◊ Logistic regression model

Table 15. Multivariable logistic regression for complications		
	Multivariable 1	**Multivariable 2**
Machine	0.83* (0.32 – 2.16)† p = 0.70◊	0.86* (0.33 – 2.26)† p = 0.77◊
*odds ratio (HR); †95.0% confidence interval (CI); ◊p-value ordered logistic regression model Multivariable 1: only adjusted for BMI Multivariable 2: adjusted for BMI and flap weight (all p<0.2)		

Diagrams

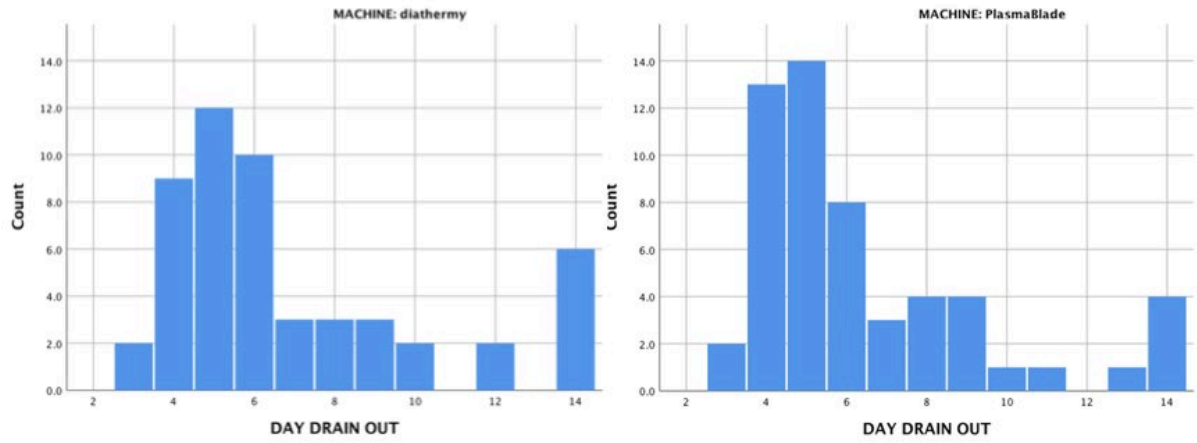

Diagram 1. Histograms for the amount of days the drains were required. On the left for the diathermy (n=52) and on the right for the PEAK PlasmaBlade™ (n=56).

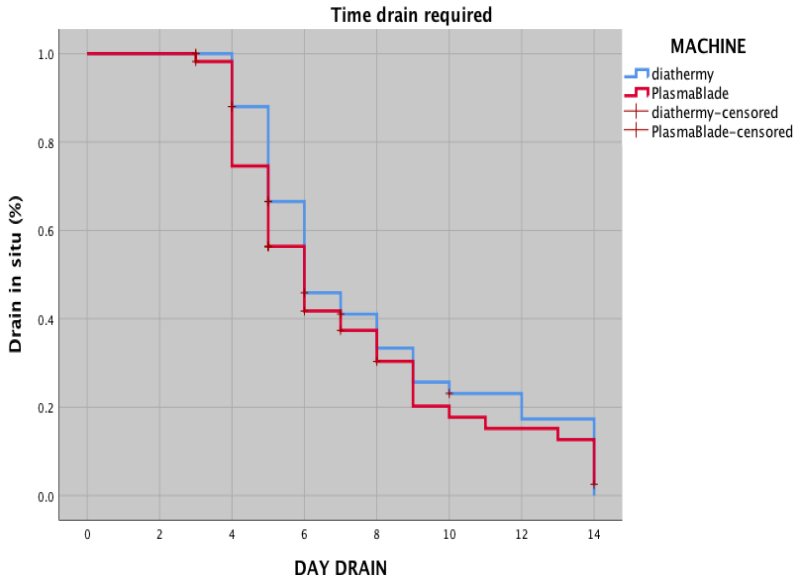

Diagram 2. Kaplan-Meier curve for the amount of days the drain was needed. Censored patients were shown with a cross.