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# Flap Fixation Using Tissue Glue or Sutures Appears to Reduce Seroma Aspiration After Mastectomy for Breast Cancer

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## Abstract

**Seroma formation and its sequelae cause complications and discomfort following mastectomy. In this retrospective study of 230 patients, patients underwent flap fixation after mastectomy using sutures or tissue glue. The results were compared to a group that had not been treated with flap fixation. The occurrence of seroma was significantly less in the group undergoing flap fixation with sutures. There were significantly fewer patients requiring seroma aspiration in both groups undergoing flap fixation.**

**Background:** Up to 90% of patients undergoing breast cancer surgery suffer from seroma formation, which can cause discomfort and various complications after mastectomy. This retrospective observational cohort study aimed to elucidate whether flap fixation with fibrin sealant (ARTISS) tissue glue reduces seroma formation and seroma aspiration after mastectomy when compared with flap fixation using Vicryl sutures and when compared with a conventional wound closure technique. **Methods:** All patients undergoing mastectomy due to invasive breast cancer or ductal carcinoma in situ were eligible for inclusion. From May 2012 to March 2013, all patients undergoing mastectomy in 2 large breast cancer centers were treated using flap fixation with Vicryl sutures. From September 2013 to March 2014, all patients undergoing mastectomy were treated with flap fixation using ARTISS tissue glue. The data were retrospectively analyzed and compared with a “drain-only” group that was not treated with flap fixation (May 2011–March 2012). **Results:** A total of 230 women who underwent mastectomy were retrospectively analyzed in this trial; 88 patients were included in the drain-only group (DO), 92 patients were included in the flap fixation group using Vicryl sutures (FF-1), and 50 patients were included in the flap fixation group using ARTISS tissue glue (FF-2). There was significantly less seroma formation in the group after flap fixation using sutures ( $P = .006$ ). There were significantly fewer patients who required seroma aspiration in the FF-1 group ( $P = .001$ ) and the FF-2 group ( $P = .001$ ) after undergoing mastectomy and sentinel node biopsy or modified radical mastectomy. **Conclusion:** This study suggests that flap fixation after mastectomy using ARTISS tissue glue or sutures reduces postoperative seroma aspiration. As a result, flap fixation might lead to less patient discomfort. A randomized, prospective trial should be performed to verify these results.

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**Keywords:** ARTISS, Breast surgery, Fluid drained, Serous fluid, Vicryl stitches

## Introduction

Seroma formation is a common complication after breast cancer surgery. The reported incidence of seroma varies between 3% to more than 90% in patients undergoing breast cancer surgery.<sup>1,2</sup>

This wide range is mostly explained by a lack of consensus on the definition of seroma and by the detection method used.<sup>3</sup> Seroma is often considered to be a surgical nuisance or a necessary evil after breast cancer surgery, which generally resolves within several weeks.

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However, it often causes discomfort and in some cases even complications, varying from delayed wound healing to infection and skin flap necrosis.<sup>1,4,5</sup> In addition to this, patients may require more frequent outpatient clinic visits for seroma and wound care.<sup>5</sup> Moreover, complications caused by infection and delayed wound healing might postpone the start of adjuvant therapy.<sup>6</sup> It is believed that reducing the dead space can prevent the accumulation of seroma. Certain prospective trials indicate that flap anchoring and therefore dead space reduction could be beneficial.<sup>7,8</sup> Drains have been demonstrated to be helpful and there also is evidence that flap fixation with sutures does reduce seroma formation.<sup>8,9</sup> In a previously conducted retrospective study by our group, flap fixation using Vicryl (polyglactin 910) sutures seemed to be an effective surgical technique in reducing dead space and therefore seroma formation and seroma aspiration in patients undergoing mastectomy for invasive breast cancer.<sup>8</sup>

ARTISS tissue glue is a fibrin sealant containing human protein and human thrombin. ARTISS is used as tissue glue to adhere/seal subcutaneous tissue in plastic, reconstructive, and burn surgery, as a replacement or an adjunct to sutures or staples. In addition, ARTISS can function as an adjunct to hemostasis on subcutaneous tissue surfaces. The fibrin adhesion system initiates the last phase of physiological blood coagulation. ARTISS is sprayed onto the skin flaps and underlying muscle, leading to adhesive fixation of the skin flap on the pectoral muscle.<sup>10</sup> ARTISS tissue glue is made of pooled human plasma. It contains 4 IU/mL thrombin leading to an extended clotting time compared with Tisseel VHSD containing 500 IU/mL thrombin. The skin graft should be attached to the wound bed immediately after ARTISS has been applied. The surgeon has up to 60 seconds to manipulate and position the graft before polymerization. Foster et al<sup>11</sup> showed that both the incidence and the extent of hematoma/seroma were significantly lower for ARTISS-treated sites than for stapled sites. The reduction in hematoma and seroma is clinically significant because of the additional procedures that are required to deal with these complications in certain cases.

Unlike Tisseel, ARTISS tissue glue is made of pooled human plasma. Flap fixation using Fibrin Glue (Tisseel) was evaluated in a Cochrane review in 2013.<sup>3</sup> The authors found no influence on the incidence of postoperative seroma formation, the mean volume of seroma, wound infections, complications, or the length of hospital stay after mastectomy for breast cancer.<sup>3</sup> However, due to a broad heterogeneity of included articles in the Cochrane review (eg, population, type of surgery), it is difficult to extrapolate these results to our group of patients.

The aim of this study was to evaluate whether ARTISS tissue glue reduces seroma formation and its sequelae when compared with flap fixation using Vicryl sutures or when compared with conventional wound closure with a drain only after mastectomy.

## Materials and Methods

This retrospective observational cohort study was conducted in the breast units of 2 large hospitals in the Netherlands (Atrium Medical Center, Heerlen, and Orbis Medical Center, Sittard). The hospitals' joint medical ethical committee granted approval (14-N-115) and informed consent was waived. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national

research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Women undergoing mastectomy for invasive breast cancer or ductal carcinoma in situ (DCIS) with or without sentinel node biopsy and modified radical mastectomy were eligible for inclusion. Direct reconstruction and breast-conserving surgery were exclusion criteria. All patients received 2 g cefazolin preoperatively. Two methods of flap fixation were applied. The method of flap fixation used depended on the period in which patients underwent mastectomy. Flap fixation using sutures (FF-1) was applied between May 2012 and March 2013. Flap fixation using ARTISS tissue glue (FF-2) was used between September 2013 and March 2014. In both groups, a low-suction drain was left in situ. The flap fixation group using ARTISS (FF-2) was compared with the flap fixation group using sutures (FF-1) and a drain-only control group (DO) that was not treated using flap fixation (May 2011-March 2012). In the control group, only a low-suction drain was left in situ. Drains were removed if fluid production was less than 50 mL/24 hours. After 7 days, all drains were removed, irrespective of drain output. Surgery was performed by 5 surgeons, all specialized in breast cancer surgery. Patients visited the outpatient clinic 1 to 2 weeks after surgery. A surgeon followed up these visits after 3 months and 1 year postoperatively. Extra visits were planned as deemed necessary.

## Surgical Techniques

In patients in the skin flap fixation group using Vicryl sutures, the skin flaps were sutured onto the pectoral muscle using polyfilament absorbable sutures (Vicryl 3.0). Vicryl sutures were placed at periodic intervals (every 3 cm) in 2 or 3 rows, depending on the extent of the skin flaps. In the group using tissue glue, ARTISS was applied as a 2-mL spray and used on both skin flaps. After the spray was applied, compression on both skin flaps to the underlying muscle was applied for 3 minutes. Intradermal skin closure using absorbable monofilament sutures (Monocryl 3.0) was applied to patients in all groups.

## Outcome Assessment

We evaluated patient characteristics of all participants using electronic medical records. Demographics of interest were as follows: age, smoking, body mass index, use of anticoagulants, and comorbidity. Seroma and seroma aspiration as well as other complications including wound infections were retrieved from the medical records. Infection was defined as any wound appearance that required antibiotic treatment or opening of the wound to evacuate infected seroma or abscess formation. Seroma was defined as a fluid collection as evidenced via palpation or clear serous fluid that was aspirated. Seroma aspirations were counted as registered in the patients' charts. Comorbidity was classified following the Charlson comorbidity index.<sup>12</sup> All oral anticoagulants were considered to be anticoagulant drugs (ie, platelet aggregation inhibitors and warfarin). Tumor stage was classified according to TNM classification.<sup>13</sup> The presence of seroma, seroma aspirations, and surgical site infections (SSI) were evaluated.

## Statistics

Statistics were performed using SPSS, version 22 (IBM Corporation, Armonk, NY). Continuous variables are presented as

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**Table 1** Patient and Operation Characteristics

	FF-2 (Glue) n = 50	DO (Drain Only) n = 88	P (FF-2 vs. DO)	FF-1 (Sutures) n = 92	P (FF-2 vs. FF-1)
Age (y)	62 (13)	69 (11)	.001	67 (13)	.04
Comorbidity	3.8 (2.2)	3.0 (1.1)	.02	2.8 (1.4)	.007
Anticoagulant drugs (yes), %	38	34	.65	25	.11
Smoking (yes), %	10	24	.04	23	.07
Tumor stage, %			.02		.03
T1-2N0	36	50		44	
T1-2N+	42	19		25	
T3	10	9		14	
T4	10	9		3	
Ductal carcinoma in situ	2	13		13	
Operation, %			.59		.56
Modified radical mastectomy	42	36		37	
Mastectomy	10	16		7	
Mastectomy sentinel node	48	48		57	
Blood loss, mL, %			<.001		<.001
0	12	37		49	
0-50	48	17		18	
50-100	24	14		19	
100-150	8	2		3	
>150	8	31		12	

means with SDs or as medians with first and third quartiles as appropriate; categorical variables are presented as percentages. Continuous variables were compared between study groups with Student's *t*-tests or Mann-Whitney *U* tests as appropriate. Categorical variables were compared between study groups with  $\chi^2$  tests or Fisher exact tests as appropriate. The risk of complications according to study group was estimated using simple logistic regression. Potential confounding by relevant baseline characteristics was corrected for using multiple logistic regression. The clinically relevant interaction between study group and operation type was assessed with the significance of the change in  $-2$  log likelihood after inclusion of the interaction term in the logistic regression models. In case of significant interaction, simple effects were reported by stratified cross-tables.  $P < .05$  was considered evidence of statistical significance.

## Results

### Patient Demographics

In total 230 patients were included; 92 in the flap fixation suture group (FF-1), 50 in the ARTISS group (FF-2), and 88 in the drain-only group (DO). Characteristics of the patients are summarized in Table 1. Women in the flap fixation suture group had significantly fewer comorbidities than in the ARTISS flap fixation group (2.8 vs. 3.8;  $P = .007$ ). Patients in the ARTISS group were significantly younger than patients in the other 2 groups (62 vs. 69;  $P = .001$ ), 62 versus 67 ( $P = .04$ ). There were fewer smokers in the ARTISS group (10%) when compared with the historical control group (24%)  $P = .04$ . Besides these characteristics, operative features were compared among the 3 groups (eg, blood loss and type of surgery: modified radical mastectomy, mastectomy, or mastectomy with sentinel node biopsy). Some clear differences in blood loss emerged,

**Table 2** Postoperative Complications

	FF-2 (Glue) n = 50	DO (Drain Only) n = 88	P	FF-1 (Sutures) n = 92	P
Any complication, %	58	64	.51	39	.03
Seroma	50	59	.30	36	.10
Seroma with aspiration	14	43	<.001	15	.85
Number of aspirations	0 (0-0)	0 (0-1)	<.001	0 (0-0)	.79
Hematoma	6	1	.14	5	.89
Surgical site infection	16	17	.87	12	.50
Pneumothorax	0	1	1.00	0	-

**Table 3** Multiple Logistic Regression Analysis

	Seroma		Seroma Requiring Aspiration	
	Odds Ratio (95% Confidence Interval)	P	Odds Ratio (95% Confidence Interval)	P
Closure technique				
Drain only (reference)	-	-	-	-
FF-2 (glue)	0.83 (0.38-1.80)	.64	0.19 (0.07-0.52)	.001
FF-1 (sutures)	0.41 (0.22-0.78)	.006	0.29 (0.14-0.61)	.001
Age (y)	1.01 (0.98-1.04)	.48	1.02 (0.99-1.05)	.28
Operation				
Mastectomy (reference)	-	-	-	-
Mastectomy and sentinel node	0.88 (0.35-2.27)	.78	0.85 (0.30-2.41)	.77
Modified radical mastectomy	1.67 (0.62-4.51)	.31	0.97 (0.32-2.90)	.95
Comorbidity (point)	0.93 (0.74-1.16)	.51	1.18 (0.91-1.55)	.22
Anticoagulant drugs (yes)	1.00 (0.50-1.97)	.99	1.10 (0.50-2.43)	.81
Smoking (yes)	1.85 (0.90-3.78)	.09	0.78 (0.34-1.79)	.55

and are listed in Table 1. There were no differences in the type of operation performed or the use of anticoagulants.

### Seroma and Complications

Postoperative complications are listed in Table 2. There was a significant difference in overall complications between the ARTISS group (58%) and the suture group (39%),  $P = .03$ . Seroma aspiration was performed in 14 (15.2%) of 92 in the suture group, in 7 (14%) of 50 in the ARTISS group, and in 52 (59.1%) of 88 in the DO group ( $P < .001$ ). Moreover, there were no significant differences in seroma aspiration between the flap fixation suture group and the flap fixation using ARTISS group ( $P = .85$ ). The number of seroma aspirations per patient who underwent seroma aspiration was also significantly reduced in both groups undergoing flap fixation (flap fixation with sutures and with ARTISS,  $P < .001$ ). No significant differences were detected in patients developing SSIs in the 3 groups.

The multiple logistic regression analysis is shown in Table 3. When analyzing the effect of method of flap closure on seroma formation, there was significantly less seroma formation in the suture group (0.41 [0.22-0.78],  $P = .006$ ) when compared with the ARTISS group (0.83 [0.38-1.80],  $P = .64$ ) and the historical control group (reference). Multivariate analysis clearly shows that flap fixation (both flap fixation with sutures and with ARTISS) is an

independent variable significantly reducing seroma aspirations ( $P < .001$ ). Smokers did not have a higher risk of seroma formation after mastectomy ( $P = .09$ ).

The effect of wound closure method on seroma formation did not change significantly with operation type (test for interaction:  $P = .15$  for seroma formation and  $P = .54$  for seroma aspiration). Exploratory analyses stratified for operation type are presented in Table 4. No effect was seen in the group undergoing mastectomy ( $P = .21$  for seroma formation and  $P = .42$  for seroma aspiration). In the group undergoing mastectomy and sentinel node biopsy, seroma formation was significantly reduced in the groups undergoing flap fixation (with sutures: 25%, with ARTISS: 38%, DO: 62%,  $P = .001$ ). Moreover, seroma aspirations also were significantly reduced in both groups undergoing flap fixation in mastectomy and sentinel node biopsy (with sutures: 14%, with ARTISS: 13%, DO: 45%,  $P = .001$ ). In modified radical mastectomy, seroma aspiration also was significantly reduced in both groups undergoing flap fixation (with sutures: 18%, with ARTISS: 14%, DO: 41%,  $P = .04$ ).

### Discussion

This retrospective study indicates that flap fixation after mastectomy and sentinel node biopsy, using sutures or tissue glue, may reduce seroma formation. Seroma aspiration was significantly

**Table 4** Effects of Flap Fixation on Seroma Formation Stratified by Operation Type

	DO (Drain Only)	FF-1 (Sutures)	FF-2 (Glue)	P
Seroma, n/N (%)				
Mastectomy	8/14 (57)	1/6 (17)	3/5 (60)	.21
Mastectomy and sentinel node	26/42 (62)	13/52 (25)	9/24 (38)	.001
Modified radical mastectomy	18/32 (56)	19/34 (56)	13/21 (62)	.89
Seroma requiring aspiration, n/N (%)				
Mastectomy	6/14 (43)	1/6 (17)	1/5 (20)	.42
Mastectomy and sentinel node	19/42 (45)	7/52 (14)	3/24 (13)	.001
Modified radical mastectomy	13/32 (41)	6/34 (18)	3/21 (14)	.04

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reduced in patients undergoing flap fixation using sutures (odds ratio [OR] 0.29 [0.14-0.61],  $P = .001$ ) and in patients undergoing flap fixation using tissue glue (OR 0.19 [0.07-0.52],  $P = .001$ ). Moreover, seroma aspiration was significantly reduced in patients undergoing flap fixation after mastectomy and sentinel node or modified radical mastectomy.

Seroma formation remains a common complication after breast cancer surgery, with an incidence of up to 90%.<sup>14</sup> Unfortunately, no means of preventing seroma are known yet. Closed suction drainage has been pivotal in the prevention of seroma, but as all surgeons know, the problem and sequelae of seroma formation still persist. Various studies have shown that flap fixation using sutures is effective in combatting seroma.<sup>8,9</sup> This is the first study to assess the effectiveness of ARTISS tissue glue in combatting seroma formation.

Flap fixation after mastectomy can be of great benefit in reducing seroma production and the number of seroma-related complications.<sup>8</sup> Flap fixation using sutures and tissue glue appears to be beneficial, as the dead space between the skin flaps and underlying pectoral muscle is reduced. Furthermore, flap fixation does not seem to influence shoulder function and/or range of motion.<sup>9</sup> Our study further indicates that seroma aspiration does not differ between the 2 methods of flap fixation.

When analyzing the interaction of operation type and method of wound closure, no significant effect was seen in seroma formation (flap fixation using sutures [17%], flap fixation using ARTISS [60%], DO [57%],  $P = .21$ ). Likewise, there were no significant differences in seroma aspiration in the group undergoing mastectomy alone (flap fixation using sutures [17%], flap fixation using ARTISS [20%], DO [43%] seroma formation,  $P = .42$ ). The low number of patients in this subgroup could explain the nonsignificance. If this group had been larger ( $n = 25$ ), the difference possibly might have been statistically significant.

Gonzalez et al<sup>15</sup> concluded that the incidence of seroma is highest after modified radical mastectomy.<sup>16</sup> Our study revealed similar results; mastectomy without lymph node dissection yields fewer cases of seroma formation when compared with modified radical mastectomy or mastectomy without (sentinel) lymph node dissection. This could possibly be explained by the fact that the remaining dead space in the axilla persists, as dead space reduction remains difficult in the axilla due to the residual 3-dimensional space in the axilla. Unfortunately, no means of preventing seroma are known yet. However, many techniques in an attempt to reduce seroma formation have been investigated, but with little avail.

## Limitations

The main limitation of this study is its retrospective nature. Indications for seroma aspiration had not been defined beforehand, and this could be considered as an information bias. In this study, the method of flap fixations was performed sequentially. Flap fixation using sutures was performed between May 2012 and March 2013, flap fixation using ARTISS was performed between September 2013 and March 2014. For that reason, it might be plausible that surgeons were more focused on establishing the

presence of seroma in the latter part of the study. The presence of seroma in the historical control group could therefore be underestimated. As no objective test is used to diagnose seroma, its presence is subject to bias. Possibly, the only true measure of seroma formation is actual seroma aspiration.

## Conclusion

In conclusion, flap fixation using ARTISS tissue glue seems to yield similar results when compared with flap fixation using sutures. Flap fixation using ARTISS tissue glue appears to lead to significantly fewer seroma aspirations in patients undergoing mastectomy and sentinel node biopsy and modified radical mastectomy for invasive breast cancer or DCIS when compared with patients without flap fixation. A prospective randomized controlled trial has been started (Seroma reduction After Mastectomy Trial) to evaluate the effects of flap fixation (no flap fixation vs. flap fixation using sutures vs. flap fixation using tissue glue), including long-term outcome measures, such as cosmesis, shoulder function, patient satisfaction, quality of life, and cost-effectiveness.

## Clinical Practice Points

- Seroma formation following mastectomy is very common and causes patient discomfort and complications.
- This study shows that flap fixation using ARTISS tissue glue appears to lead to significantly fewer seroma aspirations in patients undergoing mastectomy and sentinel node biopsy and modified radical mastectomy for invasive breast cancer or DCIS when compared with patients without flap fixation.
- There do not appear to be significant differences in seroma aspiration between the flap fixation suture group and the flap fixation group using ARTISS.
- This study formed the solid grounding of the SAM Trial, the first RCT of its kind that will evaluate the effects of flap fixation.

## Disclosure

The authors have stated that they have no conflicts of interest.

## References

1. Carless PA, Henry DA. Systematic review and meta-analysis of the use of fibrin sealant to prevent seroma formation after breast cancer surgery. *Br J Surg* 2006; 93:810-9.
2. Kumar S, Lal B, Misra MC. Post-mastectomy seroma: a new look into the aetiology of an old problem. *J R Coll Surg Edinb* 1995; 40:292-4.
3. Sajid MS, Hutson KH, Rapisarda IF, Bonomi R. Fibrin glue instillation under skin flaps to prevent seroma-related morbidity following breast and axillary surgery. *Cochrane Database Syst Rev* 2013; 5:CD009557.
4. Stehbens WE. Postmastectomy serous drainage and seroma: probable pathogenesis and prevention. *ANZ J Surg* 2003; 73:877-80.
5. Kuroi K, Shimoizuma K, Taguchi T, et al. Evidence-based risk factors for seroma formation in breast surgery. *Jpn J Clin Oncol* 2006; 36:197-206.
6. Khater A, Elnahas W, Roshdy S, et al. Evaluation of the quilting technique for reduction of postmastectomy seroma: a randomized controlled study. *Int J Breast Cancer* 2015; 2015:287398.
7. Almond LM, Khodaverdi L, Kumar B, Coveney EC. Flap anchoring following primary breast cancer surgery facilitates early hospital discharge and reduces costs. *Breast Care (Basel)* 2010; 5:97-101.
8. van Bastelaar J, Beckers A, Snoeijs M, Beets G, Vissers Y. Flap fixation reduces seroma in patients undergoing mastectomy: a significant implication for clinical practice. *World J Surg Oncol* 2016; 14:66.
9. Sakkary MA. The value of mastectomy flap fixation in reducing fluid drainage and seroma formation in breast cancer patients. *World J Surg Oncol* 2012; 10:8.
10. Inc. BLARTISS [Fibrin Sealant Human]. Deerfield: Baxter Healthcare Corporation; 2011.

11. Foster K, Greenhalgh D, Gamelli RL, et al. Efficacy and safety of a fibrin sealant for adherence of autologous skin grafts to burn wounds: results of a phase 3 clinical study. *J Burn Care Res* 2008; 29:293-303.
12. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994; 47:1245-51.
13. Sobin LH. TNM, sixth edition: new developments in general concepts and rules. *Semin Surg Oncol* 2003; 21:19-22.
14. van Bommel AJ, van de Velde CJ, Schmitz RF, Liefers GJ. Prevention of seroma formation after axillary dissection in breast cancer: a systematic review. *Eur J Surg Oncol* 2011; 37:829-35.
15. Gonzalez EA, Saltzstein EC, Riedner CS, Nelson BK. Seroma formation following breast cancer surgery. *Breast J* 2003; 9:385-8.
16. Hashemi E, Kaviani A, Najafi M, Ebrahimi M, Hooshmand H, Montazeri A. Seroma formation after surgery for breast cancer. *World J Surg Oncol* 2004; 2:44.