

A Head to Head Comparison Between SurgiMend® – Fetal Bovine Acellular Dermal Matrix and Tutomesh® – A Bovine Pericardium Collagen Membrane in Breast Reconstruction in 45 Cases

CHRISTIAN EICHLER^{1,2}, JERIA EFREMOVA¹, KLAUS BRUNNERT³, CHRISTIAN M. KURBACHER^{4,5},
OLEG GLUZ^{6,7}, JULIAN PUPPE⁵ and MATHIAS WARM^{1,5}

¹Breast Center, Municipal Hospital Holweide, Cologne, Germany;

²Department of Gynecology and Obstetrics, Municipal Hospital Holweide, Cologne, Germany;

³Department of Senology, Clinic for Senology, Osnabrueck, Germany;

⁴Clinic Center Bonn-Friedensplatz, Bonn, Germany;

⁵Department of Gynecology and Obstetrics, University of Cologne, Cologne, Germany;

⁶West German Study Group (WSG), Moenchengladbach, Germany;

⁷Breast Center Niederrhein Moenchengladbach, Moenchengladbach, Germany

Abstract. *Background/Aim:* The use of acellular dermal matrices (ADM) has become a widely used option in breast reconstruction. A great deal of literature is available, totaling over 3,200 ADM reconstructions. Head-to-head comparisons between SurgiMend® and Tutomesh® are not yet reported. These are the first comparative clinical data reported on the use of Tutomesh® in breast reconstruction. *Postoperative complication rates and costs for these devices were evaluated. Patients and Methods:* This is a retrospective analysis of a 2-year experience with both SurgiMend® - fetal bovine acellular dermal matrix and Tutomesh® - a bovine pericardium collagen membrane in breast reconstruction in 45 cases from 2014-2015. *Results:* Forty-five patients received a total of 45 implant-based reconstructions using SurgiMend® (18 cases; 40%) or Tutomesh® (27 cases; 60%). Gross complication rates were 27.8% for SurgiMend® and 37.0% for Tutomesh® including hematoma, postoperative skin irritation, infection, red breast syndrome and revision surgery. The most common complication was postoperative red breast syndrome. Severe

complications requiring revision surgery did not differ significantly in patients treated with SurgiMend® (0 cases, 0%) compared to Tutomesh® (1 case, 3.7%). *Conclusion:* This retrospective analysis shows similar overall clinical complication rates for Tutomesh® and SurgiMend®. Severe complication rates are comparable to those reported in literature for both products. Although the retrospective nature of this work limits its clinical impact, it is possible to opt for the cheaper alternative (Tutomesh®).

Several different approaches are available for breast reconstruction in a post-oncological scenario. Most of them still involve implant-based procedures. This is due to the fact that implant-based reconstruction is a less invasive option when compared to autologous approaches as there is generally a decrease in morbidity but also it being the most cost-effective method (1-3). Current available literature shows that implant-based reconstruction is used in 37% of breast cancer patients (4, 5). While the initial goal of all breast reconstructions should always be a satisfying aesthetic outcome as well as a low complication rate procedure, financial concerns become more of an issue in the German health care system. This is due to a reimbursement system and the public health sector where the reimbursement envelope is based on the German DRG (Diagnosis Related Groups) system. While attempting to reach the optimal outcome for the patient, this reimbursement system does not allow for additional surgical cost factors to be reimbursed. This is especially true for Acellular dermal matrix (ADM) supported reconstruction. When the decision is made to apply ADM supported reconstruction the financial disadvantage remains

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Correspondence to: Dr. med. Christian Eichler, Breast Center, Municipal Hospital Holweide, Neufelder Str. 32, 51067 Cologne, Germany. Tel: +49 1635050614, e-mail: ceichler@gmail.com, eichlerc@kliniken-koeln.de

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with the hospital. Nonetheless, there are often circumstances which require ADM support in heterologous reconstruction scenarios. The overall financial benefit of introducing additional material into a subcutaneous reconstruction is still under investigation (6). Most often ADMs are used in a skin-sparing mastectomy (SSM) situation. Additional applications include for example heterologous breast augmentation with a sub-pectoral implant pocket as fixation of the pectoralis major muscle. Their use has become an attractive, but expensive option. Approximately 3,200 ADM reconstructions have been discussed in the literature as of 2016 (both synthetic and biological). A new alternative to commonly used ADMs is Tutomesh® a bovine pericardium collagen membrane. This material is most commonly used in hernia repair scenarios (7). Data from only 24 breast reconstructions are available for this material (8). However, these data were not comparative in nature. In order to establish comparability however, analysis requires the inclusion of an ADM previously investigated. Therefore, Tutomesh® has been retrospectively compared to SurgiMend®. All current data on this material are also retrospective. As always, in implant-based reconstruction eventual prior or subsequent radiotherapy may lead to a substantial decrease in overall outcome (9) and should therefore also be recorded.

These are the first comparative clinical data reported on the use of Tutomesh® in breast reconstruction. Postoperative complication rates and costs for these devices were evaluated.

Patients and Methods

This analysis is a retrospective review of a single center experience, 2014 to 2016, with both SurgiMend® - fetal bovine acellular dermal matrix and Tutomesh® - a bovine pericardium collagen membrane in breast reconstruction in 45 cases. Surgical interventions included both oncological and plastic subcutaneous mastectomies. 45 patients had immediate implant based reconstructions. There was no prospective trial recruitment situation. ADMs were used whenever necessary. ADM choice was based purely on the availability. The first 18 patient received SurgiMend® based reconstructions. The following 27 patients received Tutomesh® reconstruction. Patient recruitment was therefore non-randomized, consecutive and non-biased.

Endpoints. Retrospective analysis endpoints included post-surgical red breast syndrome (RBS – redness exceeding normal postoperative redness), seroma requiring aspiration, infection requiring intravenous (*i.v.*) antibiotics, and revision surgery (with implant loss). These endpoints are commonly used in the evaluation of ADMs (10). RBS was considered a mild, transient complication, which is often mistaken for an infection and unnecessarily treated with antibiotics although this hypersensitivity better responds to corticosteroids (11). It may also simply resolve itself, without additional intervention. Seroma requiring aspiration and infection requiring *i.v.* antibiotic treatment were also categorized as a mild complication. Revision surgery with implant loss (due to wound dehiscence, hematoma, antibiotic resistant infection *etc.*) was considered a severe complication.

SurgiMend®. SurgiMend® PRS (TEI, Biosciences, Inc., Boston, MA, USA) is derived from fetal bovine dermal collagen (Figure 1). Apart from advantageous mechanical properties (12), the manufacturer states it to be rich in type III collagen which may mediate tissue healing while inhibiting scarring (13). It may also not elicit an acute or chronic foreign body inflammatory response thus eliminating degeneration of the implant site. Furthermore, its microporous matrix is rapidly re-vascularized which in turn may support tissue-building and healing for prolonged reinforcement (14). This mesh is fenestrated, theoretically allowing fluid accumulations around the implant to drain into the surrounding tissue (15). A PubMed search currently (2/2017) lists 10 publications regarding the SurgiMend® ADM. Four of them include retrospective analyses in breast reconstructions.

Tutomesh®. Tutomesh® is an avital, acellular, xenogenic collagen membrane made from bovine pericardium (Figure 2) (Tutogen Medical GmbH, 91077, Neunkirchen am Brand, Germany). The manufacturer states that Tutomesh® consists of 92% native collagen type I, which maintains in its three-dimensional structure, therefore being extremely resistant to tensile forces. This ADM, similar to SurgiMend® allows in-growth of vessels and fibroblasts, thereby being gradually replaced by the patient's own tissue. Very little data is available in breast reconstruction in this area. A PubMed search currently (2/2017) lists one publication regarding the Tutomesh® ADM.

Surgical technique. Surgery was performed according to the gold standard for SSM/NSM immediate implant-based reconstruction. All surgeries were performed by experienced senological surgeons. All materials were handled according to the manufacturer's specifications. Antibiotics were administered during surgery. No antibiotics were given after surgery unless required by clinical parameters. Drains were not removed within the first 24 h post-surgical period. Thereafter, a threshold of 30 ml/24 h was used as a cutoff for maintaining drainage. Surgical compression bras were applied immediately after surgery and worn by the patient for at least a 6 week period.

Informed consent. Written informed consent was obtained from all patients. A copy of the written consent is available for review. This study was conducted in accordance with institutional review board standard operating procedures.

Ethics committee approval. This study was conducted in accordance with institutional review board standard operating procedures. An ethics committee vote was initiated, but deemed unnecessary by the "Ethikkommission der Ärztekammer Nordrhein". A written statement is available.

Statistics. Statistical analysis was performed using the VassarStats® (Vassar College, Poughkeepsie, NY, USA) statistics program. ANOVA analysis and *t*-tests were used in order to evaluate significances when appropriate.

Results

Forty-five patients received a total of 45 implant-based reconstructions using SurgiMend® (18 cases; 40%) or Tutomesh® (27 cases; 60%). An overview is given in Table I.

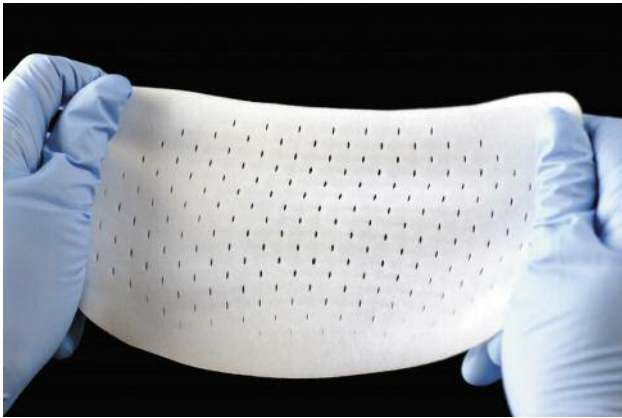


Figure 1. SurgiMend® PRS (TEI, Biosciences, Inc., Boston, MA, USA) is derived from fetal bovine dermal collagen. This image shows a fenestrated 10×15 cm ADM.



Figure 2. Tutomesh® (Tutogen Medical GmbH, 91077, Neunkirchen am Brand, Germany). The image shows the fenestrated equivalent to Figure 1.

Intergroup comparability is given. All procedures were subcutaneous mastectomies with or without prior radiation treatment. Most of the interventions were oncological interventions for both groups; SurgiMend® (17 cases-94.4%) and Tutomesh® (24 cases-88.9%). The median age for the SurgiMend® group was 49.8 years (range=23-72) and the median age for the Tutomesh® group was 49.5 years (range=34-69); two sided *t*-test $p=0.41$). The median BMI for Tutomesh® group was 22.6 (range=18-33) and 22.4 (Range=17-34 for the Tutomesh® group (two sided *t*-test $p=0.19$). Inter-group comparability is given.

Gross minor complication rates were 27.8% for SurgiMend® and 37.0% for Tutomesh® including hematoma, postoperative skin irritation, infection, red breast syndrome and revision surgery (not statistically different $p=0.75$). The most common complication was postoperative red breast syndrome with 16.7% in the Strattice® group and 14.8% in the Tutomesh® group. Postoperative infections were treated in 5.6% (1 case-SurgiMend®) and 18.5% (5 cases-SurgiMend®) of all surgeries. This difference is not statistically significant ($p=0.42$). Only one severe complication requiring revision surgery occurred. Results include revision within the first 30 days after surgery. Revision with implant loss was not performed in the SurgiMend® group compared to a single revision in the Tutomesh® group (1 case, 3.7%). This was due to an infection which could not be sufficiently treated with antibiotics. Implant and Tutomesh® ADM removal followed. Subsequent re-reconstruction followed without any complications. Subsequent revision due to capsular contracture or oncological reasons occurred in 22.2% (SurgiMend®) and 22.5% (Tutomesh®) of all cases.

Discussion

Although the use of ADMs may at times be a necessity, it remains thoroughly unclear which product should be used. Initially, the general consensus was that different ADM products may lead to varying complication rates. Over the last decade however it has become apparent that different ADMs do not represent an independent risk factor (16). While prospective randomized trials comparing different products in a long-term scenario are still missing, the body of retrospective analyses is ever-growing. Also, large meta-analyses are available suggesting no or very little (prior radio-therapy) difference in complication rates with different ADM products. However, smoking, age, and initial tissue expander fill volume are still associated with increased risk of postoperative complications (17, 18). Despite the assumption that ADM type may not be an independent risk factor, it remains important to compare new products to existing data. Including this work there are only 5 available publications regarding the use of SurgiMend®, and Tutomesh® in breast reconstruction (Table II) (8, 10, 16, 19). Within these studies, head to head comparisons were made to AlloDerm® and Epiflex®; both products based on human tissue. Of those four products, AlloDerm® is the most thoroughly investigated. Implant loss data shown in Table II represent a good estimation of its representation in literature.

While complications such as red breast syndrome, infection, hematoma and seroma may be problematic in a postsurgical management, the main concern remains implant loss and subsequent increased patient morbidity as well as increasing costs. Figure 3 shows a pooled analysis of complication rate data for SurgiMend®, Epiflex® and

Table I. Patient demographics and overall results.

	SurgiMend®		Tutomes®		p-Value*
	n	%	n	%	
Patients	18		27		
Oncological Intervention	17	94.4	24	88.9	0.92
Aesthetic Surgery	1	5.6	3	11.1	
Smoking	3	16.7	8	29.6	
Chemotherapy	10	55.6	18	66.7	
Radiation	9	50.0	14	51.8	
Diabetic	1	5.6	0	0	0.53
Average Age	49.8±12.3		49.5±9.8		0.41
Average BMI	22.6±3.4		22.4±3.6		0.19
Complications	5	27.8	10	37.0	0.75
Post Operative Redness**	3	16.7	10	27.7	0.25
Red Breast Syndrome	3	16.7	4	14.8	
Seroma requiring aspiration	0	-	0	-	
Infection requiring i.v. antibiotics	1	5.6	5	18.5	0.42
Hematoma	1	5.6	0	-	0.84
Immediate Revision Surgery***	0	-	1	3.7	0.81
Subsequent Revision Surgery****	4	22.2	6	22.5	0.79

*Pearson Chi-squared, Fisher's exact probability test, or *t*-test (two-tailed) whenever appropriate. **Overall Postoperative Redness - no intervention required. ***Revision surgery due to wound dehiscence, hematoma etc. (within 30 days). ****Revision surgery due to Capsular contracture, tumor recurrence etc. (more than 6 months post OP).

Table II. Current available data on SurgiMend®, Tutomes® and Epiflex in breast surgery (PubMed Search, February 2017). All data are retrospective. All reconstructions were immediate and implant based.

Author	Year	ADM	Source	n	Result	Implant loss	Cost US \$
Butterfield <i>et al.</i>	2013	SurgiMend®	Bovine	351	AlloDerm® vs. SurgiMend®; no major difference	8.3% (29)	\$ 2816
Eichler <i>et al.</i>	2015	SurgiMend®	Bovine	63	SurgiMend® vs. Epiflex®, no major difference	4.8% (3)	\$ 2485
Ricci <i>et al.</i>	2016	SurgiMend®	Bovine	374	AlloDerm® vs. SurgiMend®; no major difference	2.6% (10)	\$ 2816
Eichler <i>et al.</i>	2017	SurgiMend®	Bovine	18	Tutomes® vs. SurgiMend®, no major difference	0% (0)	\$ 2485
Butterfield <i>et al.</i>	2013	AlloDerm®	Human	89	AlloDerm® vs. SurgiMend®; no major difference	11.2% (10)	\$ 3840
Ricci <i>et al.</i>	2016	AlloDerm®	Human	578	AlloDerm® vs. SurgiMend®; no major difference	2.9% (17)	\$ 3840
Eichler <i>et al.</i>	2015	Epiflex®	Human	64	SurgiMend® vs. Epiflex®, no major difference	12.5% (8)	\$ 2230
Gubitosi <i>et al.</i>	2014	Tutomes®	Bovine	28	Single arm study, safe to use, no comparison	4.2% (1)	\$ 801
Eichler <i>et al.</i>	2017	Tutomes®	Bovine	27	Tutomes® vs. SurgiMend®, no major difference	3.7% (1)	\$ 801
Total	Years 2013-2017			1592	Implant Loss Overall=3.29%±3.9		

Available Data on SurgiMend®, Tutomes® and Epiflex in Breast Surgery (Feb. 2017), all retrospective, all immediate reconstruction. Pricing is as publicly listed or as presented in publication.

Tutomes® (10). We found complication rates to be low and comparable to literature in all cases. An implant loss rate of 3.7% (SurgiMend®), 12.5% (Epiflex®) and 3.7% (Tutomes®) is comparable to current AlloDerm® implant loss data 2.9%-11.2%. It is also important to realize that most of these interventions were of an oncological nature

and that when extending a postsurgical follow-up beyond a six month window, implant loss or revision rates increase significantly by 22.2% (SurgiMend®) and 22.5% (Tutomes®) (Table I). The main reason was capsular contracture and/or tumor recurrence. Neither of those two problems seems to be caused by the ADM.

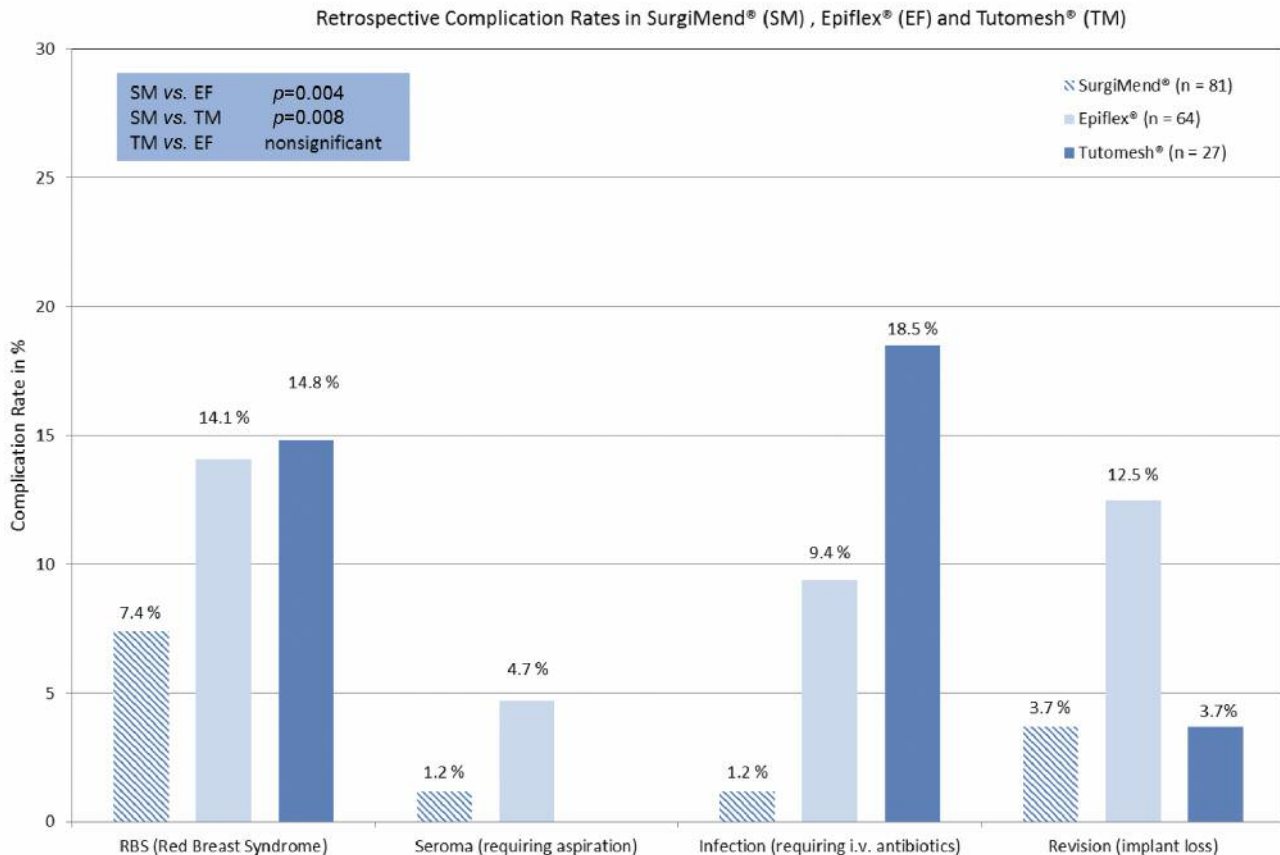


Figure 3. Retrospective complication rates for SurgiMend®, Epiflex® and Tutomesh®. SurgiMend® data have been pooled with (10) in order to increase the number of samples (n). Epiflex® data was also first presented in (10). Tutomesh® data was collected in this trial only.

Although low in numbers these results strengthen the overall notion that ADM type may not be a solid independent risk factor. Again, this needs to be evaluated in a prospective randomized trial and no definitive recommendation can be made at this point in time. While low patient morbidity should be a primary concern, the financial factor must not be ignored. Of all available products, Tutomesh® offers the cheapest alternative. While pricing may of course vary, official Tutomesh® list price is often less than half of the price of the competing products. At similar complication rates, we suggest that one should opt for this material when performing ADM supported implant breast surgery (Table II). This is especially true in a medical reimbursement system which is based on the German DRG system where additional surgical costs are not directly reimbursed.

Conclusion

This retrospective analysis shows similar overall clinical complication rates for Tutomesh® and SurgiMend®. It is the only head-to-head comparison of Tutomesh® in breast

surgery available today. Severe complication rates are comparable to those reported in literature for both products. Although the retrospective nature and limited numbers of this work limits its clinical impact, Tutomesh® offers a viable and cost effective option in ADM supported breast reconstruction.

References

- 1 Soong IS, Yau TK, Ho CM, Lim BH, Leung S, Yeung RM, Sze RM and Lee AW: Post-mastectomy radiotherapy after immediate autologous breast reconstruction in primary treatment of breast cancers. *Clin Oncol (R Coll Radiol)* 16: 283-289, 2004.
- 2 Spear SL, Parikh PM, Reisin E and Menon NG: Acellular dermis-assisted breast reconstruction. *Aesthetic Plast Surg* 32: 418-425, 2008.
- 3 Spear SL and Pelletiere CV: Immediate breast reconstruction in two stages using textured, integrated-valve tissue expanders and breast implants. *Plast Reconstr Surg* 113: 2098-2103, 2004.
- 4 Albornoz CR, Bach PB, Mehrara BJ, Disa JJ, Pusic AL, McCarthy CM, Cordeiro PG and Matros E: A paradigm shift in U.S. Breast reconstruction: increasing implant rates. *Plast Reconstr Surg* 131: 15-23, 2013.

- 5 Dieterich M, Paepke S, Zwiefel K, Dieterich H, Blohmer J, Faridi A, Klein E, Gerber B and Nestle-Kraemling C: Implant-based breast reconstruction using a titanium-coated polypropylene mesh (TiLOOP Bra): a multicenter study of 231 cases. *Plast Reconstr Surg* 132: 8e-19e, 2013.
- 6 Bank J, Phillips NA, Park JE and Song DH: Economic analysis and review of the literature on implant-based breast reconstruction with and without the use of the acellular dermal matrix. *Aesthetic Plast Surg* 37: 1194-1201, 2013.
- 7 Nedelcu M, Verhaeghe P, Skalli M, Champault G, Barrat C, Sebbag H, Nedelcu M, Verhaeghe P, Skalli M, Champault G, Barrat C, Sebbag H, Reche F, Passebois L, Beyrne D, Gugenheim J, Berdah S, Bouayed A, Michel Fabre J and Nocca D: Multicenter prospective randomized study comparing the technique of using a bovine pericardium biological prosthesis reinforcement in parietal herniorrhaphy (Tutomech TUTOGEN) with simple parietal herniorrhaphy, in a potentially contaminated setting. *Wound Repair Regen* 24: 427-433, 2016.
- 8 Gubitosi A, Docimo G, Parmeggiani D, Pirozzi R, Vitiello C, Schettino P, Avellino M, Casalino G, Amato M, Ruggiero R and Docimo L: Acellular bovine pericardium dermal matrix in immediate breast reconstruction after Skin Sparing Mastectomy. *Int J Surg* 12(Suppl 1): S205-208, 2014.
- 9 Ng CE, Pieri A and Fasih T: Porcine acellular dermis-based breast reconstruction: complications and outcomes following adjuvant radiotherapy. *Eur J Plast Surg* 38: 459-462, 2015.
- 10 Eichler C, Vogt N, Brunnert K, Sauerwald A, Puppe J and Warm M: A Head-to-head Comparison between SurgiMend and Epiflex in 127 Breast Reconstructions. *Plast Reconstr Surg Glob Open* 3: e439, 2015.
- 11 Ganske I, Hoyler M, Fox SE, Morris DJ, Lin SJ and Slavin SA: Delayed hypersensitivity reaction to acellular dermal matrix in breast reconstruction: the red breast syndrome? *Ann Plast Surg* 73(Suppl 2): S139-143, 2014.
- 12 Deeken CR, Eliason BJ, Pichert MD, Grant SA, Frisella MM and Matthews BD: Differentiation of biologic scaffold materials through physicochemical, thermal, and enzymatic degradation techniques. *Ann Surg* 255: 595-604, 2012.
- 13 Gaster RS, Berger AJ, Monica SD, Sweeney RT, Endress R and Lee GK: Histologic Analysis of Fetal Bovine Derived Acellular Dermal Matrix in Tissue Expander Breast Reconstruction. *Ann Plast Surg* 70(4): 447-453, 2013.
- 14 TEI B: Inc., Boston, MA, USA (access: 08.2014) <http://www.teibio.com/products/by-brand/surgimend/>.
- 15 Dieterich M and Faridi A: Biological Matrices and Synthetic Meshes Used in Implant-based Breast Reconstruction – a Review of Products Available in Germany. *Geburtshilfe Frauenheilkd* 73: 1100-1106, 2013.
- 16 Ricci JA, Treiser MD, Tao R, Jiang W, Guldbrandsen G, Halvorson E and Chun YS: Predictors of Complications and Comparison of Outcomes Using SurgiMend Fetal Bovine and AlloDerm Human Cadaveric Acellular Dermal Matrices in Implant-Based Breast Reconstruction. *Plast Reconstr Surg* 138: 583e-591e, 2016.
- 17 Macarios D, Griffin L, Chatterjee A, Lee LJ, Milburn C and Nahabedian MY: A Meta-analysis Assessing Postsurgical Outcomes between Aseptic and Sterile AlloDerm Regenerative Tissue Matrix. *Plast Reconstr Surg Glob Open* 3: e409, 2015.
- 18 Sobti N and Liao EC: Surgeon-Controlled Study and Meta-Analysis Comparing FlexHD and AlloDerm in Immediate Breast Reconstruction Outcomes. *Plast Reconstr Surg* 138: 959-967, 2016.
- 19 Butterfield JL: 440 Consecutive immediate, implant-based, single-surgeon breast reconstructions in 281 patients: a comparison of early outcomes and costs between SurgiMend fetal bovine and AlloDerm human cadaveric acellular dermal matrices. *Plast Reconstr Surg* 131: 940-951, 2013.

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