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Biosynthetic cellulose compared to porcine xenograft in the treatment of partial-thickness burns: A randomised clinical trial

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ABSTRACT

Aim: The aim was to compare two dressing treatments for partial-thickness burns: biosynthetic cellulose dressing (BsC) (Epiprotect® S2Medical AB, Linköping, Sweden) and porcine xenograft (EZ Derm®, Mölnlycke Health Care, Gothenburg, Sweden).

Methods: Twenty-four adults with partial-thickness burns were included in this randomized clinical trial conducted at The Burn Centers in Linköping and Uppsala, Sweden between June 2016 and November 2018. Time to healing was the primary outcome. Secondary outcomes were wound infection, pain, impact on everyday life, length of hospital stay, cost, and burn scar outcome (evaluated with POSAS).

Results: We found no significant differences between the two dressing groups regarding time to healing, wound infection, pain, impact on everyday life, duration of hospital stay, cost, or burn scar outcome at the first follow up. Burn scar outcome at the 12-month follow up showed that the porcine xenograft group patients scored their scars higher on the POSAS items thickness ($p = 0.048$) and relief ($p = 0.050$). This difference was, however, not confirmed by the observer.

Conclusions: The results showed the dressings performed similarly when used in adults with burns evaluated as partial thickness.

1. Introduction

Pre-meshed porcine xenografts have been used for more than 50 years as a primary dressing for burns treated conservatively [1,2]. Porcine xenografts have several benefits as they have been associated with low infection rates, decreased pain, fewer dressing changes, faster re-epithelialization, and minimized loss of fluid and heat [1–6]. Concerns have been raised regarding the use of

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animal products in general and porcine in particular, and the potential risk of transmitting diseases between species [7–10]. Other dressing alternatives with similar characteristics have been developed over the years. A dressing of specific interest is the biosynthetic cellulose (BsC), a polymer synthesized in abundance by *Acetobacter xylinum* which was investigated previously by the study center [11]. The BsC presents high water absorption capacity, resistance to degradation, and good permeability. Most of these properties arise from BSc's three-dimensional nanofibrillar network [12,13]. Adipose stem cells, dermal fibroblasts, and human umbilical vein endothelial cells (HUVEC) have shown good proliferation and no difference in morphology when cultured adjacent to, or attached to, BsC [14,15].

In partial-thickness burns both the porcine xenograft and the BsC dressings allow re-epithelialization underneath the dressing. As the skin is re-epithelialized, the dressing dries out and can be peeled off, or detaches spontaneously, within approximately two weeks. In areas of deep dermal or full thickness burns the dressings will not adhere and will rapidly (within days) be sloughed off. In this aspect the dressings can be considered also as a diagnostic tool when it is difficult to determine burn depth [11,14,16].

This study aims at comparing the clinical performance of biosynthetic cellulose and porcine xenograft for the treatment of partial-thickness burns in adults. Time to healing was the primary outcome. Secondary outcomes were wound infection, pain, impact on everyday life, cost, length of hospital stay, and burn scar outcome (evaluated with POSAS).

2. Patients and methods

This study was approved by the Swedish Ethical Review Authority (2016/26-31) and is registered at ClinicalTrials.gov (NCT04412759, MC-2015).

2.1. Trial design and study participants

This prospective open randomized clinical trial (RCT) included 24 adults (>18 years) admitted to the burn centers in Linköping or Uppsala, Sweden between June 2016 and November 2018.

Study participants who had been admitted within 72 h of injury with partial-thickness burns (according to the primary evaluation of the plastic surgeon on duty on both study sites) that had received a temporary wound cover were eligible and enrolled after oral and written informed consent had been obtained. Adults with any other serious trauma to the skin, chronic or current skin disease, severe cognitive dysfunction or psychiatric disorder, and pregnant or breast-feeding women were excluded.

2.2. Interventions and randomization

On admission, the patients were examined by an experienced burn surgeon who evaluated the depth of the burn examining pain sensation, color, and capillary refill as well as the extent of the burn using a Lund and Browder chart [17,18]. Burn depth was judged as either superficial dermal, deep dermal, or full thickness. The burn surface area was recorded as the percentage of the total body surface area (TBSA %).

Burns estimated as full thickness or located on soles, palms, genitalia, or face/head were not included in the study. In Table 1 the study participants TBSA % and the study-included TBSA % is described.

After patients had given consent to participate in the study and eligibility was checked an envelope containing the randomly assigned dressing treatment was opened. The envelopes, created externally before study start, were stored in the patient's file marked with the assigned study number (given in consecutive order).

At admission and at all dressing changes the wounds were cleaned with saline solution before obtaining microbial swabs and photographs, and the study dressing was applied under clean or sterile conditions. Blood samples of capillary

Table 1 – Details of the patients by dressing treatment.

	Porcine Xenograft (n = 11)	BsC (n = 13)	p Value
Sex (male/female)	10/1	12/1	1.0
Age, years (min–max)	50 (25–57)	30 (19–73)	0.082
Body mass index (10-90th centiles)	**30 (24–46)**	**24 (19–33)**	**0.007**
Patients with previous illnesses	2*	4**	0.649
Smokers	4	2	0.357
Burn			
Flame/scald/contact	8/2/1	7/6/0	0.232
TBSA%:	12 (4–31)	7 (3–62)	0.331
Superficial dermal	5 (0–15)	5 (0–50)	0.865
Deep dermal	1 (0–12)	0 (0–10)	0.733
Full thickness	0 (0–3)	0 (0–15)	0.732
TBSA % included in study	9 (2–14)	5 (1–16)	0.228
Patients with operations	5	5	1.0

Data are number, or median (10–90 centiles) unless otherwise stated. *One patient had hypertension and dyslipidemia and one had asthma and anxiety disorder. **Three patients had hypertension, one of these also suffered from kidney failure, atrial fibrillation, and diabetes mellitus. One additional patient had diabetes mellitus.

C-reactive protein were drawn on enrollment day (day 0–2), after 3–5 days, and finally after 6–8 days (depending on specific visit days).

According to clinical practice, burns that were later evaluated as deep dermal or full-thickness burns in the regular dressing change procedures by the attending plastic surgeon were excised and skin grafted. Surgical details from these procedures were noted in the case report form.

Participants undergoing surgery on study-included burns continued in the study until all included wounds were healed, regardless of surgery or dressing used during the study.

2.3. Study dressings

The dressings compared in this study were biosynthetic cellulose (BsC; Epiprotect®, S2 Medical AB, Linköping, Sweden) and porcine xenograft (EZ Derm®, Mölnlycke Health Care, Gothenburg, Sweden). The dressings were applied after the wound was carefully cleansed with normal saline. It was cut to overlap the extent of the burn onto unburned skin and held in place with either a dermal glue, staples, or sutures according to the clinical routine at the site.

The BsC was covered with two layers of paraffin gauze (Jelonet® Smith & Nephew UK Limited, London, UK) and several layers of dry gauze. Dressings were held in place using elastic tubular dressings. The porcine xenograft was covered with a layer of a polyethylene net (Dermanet® DeRoyal, Tennessee, USA) or paraffin gauze and several layers of dry gauze.

Study dressings were examined 2–5 days after application and after that weekly until complete healing. Healing time, wound infection, pain, impact on everyday life, length of hospital stay, burn scar outcome, and (local) adverse events were recorded in the case report form. The dressings were to remain intact on the wound surface until spontaneous separation whilst the paraffin gauze or polyethylene net was changed each time the patient was followed up.

Study participants were either hospitalized or attended the outpatient clinic depending on the severity of the injury. Participants discharged from hospital were instructed to report to the burn center if any problems developed with the dressings, or if any signs of infection or any other deteriorating symptoms developed.

2.4. Primary outcome

2.4.1. Healing time

Healing time was defined as the number of days from the day of the injury to when the wound was judged by the treating burn surgeon as being epithelialized to ≥95%. At all visits the burn surgeon on duty evaluated the surface (% TBSA) of the wound that was healed.

As study dressings have different appearance and adheres to the wound bed until spontaneous separation, no blinded evaluation was possible. On areas of the wound that were still healing study dressing was left whereas healed parts (where study dressing had come off) were protected from shearing according to the clinical routine at each study site in the same manner in both groups.

2.5. Secondary outcomes

2.5.1. Burn wound infection

The treating burn surgeon diagnosed wound infection if at least two of the following criteria, based on the definition of burn wound infection stated by the American Burn Association, were fulfilled [19,20,21]:

Burn wound exhibits clinical signs locally such as spreading erythema, heat, swelling or pain.
Wound swab showed positive bacterial growth.
Increase in C-reactive protein concentration (>10 mg/L) combined with increased body temperature with other infection foci ruled out.

If infection was suspected in the wound, initial treatment with topical antimicrobials (e.g. silver sulfadiazine) and/or systemic antibiotics (sort decided by treating physician) was administered. If infection developed, the patient continued in the study. Infection of the burn, regardless of dressings used, was not noted as an adverse event.

2.5.2. Pain

A numerical rating scale (NRS) ranging from 0 to 10 was used by the patients to estimate pain during dressing change, activity, and rest. A score of 0 indicates no pain and 10 worst imaginable pain.

2.5.3. Impact on everyday life

In a similar manner, an NRS scale was used to evaluate the impact on everyday life where 0 corresponds to no impact and 10 equals worst imaginable impact [4]. If patient scored the impact more than 0 they were also asked to give details about what affected them. In these cases, the Observer would suggest possible causes so that the patient could confirm or reject that specific cause. These possible causes that the Observer suggested were: smell, pain, impaired mobility, difficulties in getting dressed, and leakage of dressing. Patients were also asked to state any other cause that the patient could think of.

2.5.4. Length of hospital stay (LOS)

All patients hospitalized for their burns were monitored by the study nurse and the day of discharge was noted in the case report form. Any readmission after initial discharge was also noted and included in the total length of stay.

2.5.5. Cost

The cost of study dressings was calculated from the square centimeters of dressing used per treated TBSA%, multiplied with the price per square centimeter for each dressing.

The two secondary dressings used were similar in cost at the time of the study. The price for the polyethylene net was approximately $ 0,0018 per square centimeter and the paraffin gauze $ 0,0016 per square centimeter, hence tno difference was seen in secondary dressing costs

2.5.6. Burn scar outcome

All study participants were asked to come back to the burn centers for a scar follow-up at six and 12 months after injury. Burn scar outcome was evaluated using the Patient Observer Scar Assessment Scale (POSAS). The scale includes two

separate subscales, The Observer Scale, used by an experienced burn occupational therapist and the Patient Scale, used by the study participant.

POSAS is a commonly-used and validated scale for evaluating scars. The Observer scores six items: pigmentation, vascularity, thickness, pliability, relief, and surface area. The Patient Scale contains six questions that addresses the items: itching, pain, thickness, stiffness, color, and relief. For both the Patient and the Observer the scores for each item is added (1–10 where 10 indicates the worst imaginable sensation or scar and 1 corresponds to normal skin). Moreover, for the Observer nominal variables, such as type of pigmentation, may be recorded in category boxes in addition to the 10 point scale. Lastly, the Patient and Observer score their "Overall Opinion" of the scar compared to normal skin with the same 10 point scale, where 1 is normal skin and 10 is the most markedly different scar [22,23].

2.5.7. *Safety*

Research subjects were routinely questioned about adverse events at study visits. The adverse events were limited to application site reactions (and surrounding skin) since the products are CE-marked and used for the indications suggested by the manufacturers. Patients were monitored/observed for infection (and sepsis) as one of the outcomes in the study.

Any adverse event was recorded in the medical record and in the case report form.

2.6. *Sample size*

One of the primary outcome measures was days until complete wound epithelialization (≥95%). Previous data in burn patients treated with porcine xenograft showed re-epithelialization within a mean (SD) of 15 (4) days and a minimally clinically important difference was set to 3 days. Thus, sample size was calculated to 26 at 80% power with an α of 0.05. (S/N ratio = 0.75).

2.7. *Withdrawal criteria*

Participation in the study was voluntary and participants had the right at any time, without specific explanation, to interrupt participation. Already acquired data were analyzed if the participant did not disapprove. Removed participants were not replaced. If a patient was removed from the study, he or she received treatment according to the standards of care in the specific burn center.

2.8. *Blinding*

Since both study dressings have very different and specific characteristics, study treatments could not be blinded, and the study was to be performed in an open manner. Evaluation of all outcomes was therefore made in an open manner, except for the evaluation of burn scar outcome.

2.9. *Statistics*

For the statistical analysis SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) was used. As the sample size was relatively small and as many of the variables were qualitative a normal distribution could neither be assumed nor tested. The Mann–Whitney *U*-test and the chi squared test or Fisher's exact test (as appropriate) was used to evaluate the significance of any differences between the two groups. Probabilities of <0.05 were accepted as significant. The results are presented as median (10th–90th centiles) except for the variables healing time, age, and impact on everyday life that are presented with median (min–max). Data were analyzed on an intention to treat (ITT) basis.

3. Results

Twenty-six adults with partial-thickness burns were enrolled in the study, two participants chose to withdraw and declined analysis of all data. Data for the remaining 24 participants were reported. Twenty-two (91.7%) of the participants were male. The group had a median age of 39 (19–73) years. Most common cause of burn was flame (n = 15, 62.5%), followed by scalds (n = 8, 33.3%), and contact burns (n = 1, 4.2%). Median percentage of TBSA burned was 11 (4–37) % and the median TBSA treated with study dressings was 7 (2–14) %. Eleven participants were randomized to treatment with porcine xenograft and 13 to BsC. Regarding sex distribution, age, previous illnesses, smoking habits, TBSA % burned, TBSA % treated with study dressing, depth of burn, and number of patients undergoing surgery the two groups did not differ, but participants in the porcine xenograft group had a significantly higher body mass index (BMI) and a tendency (p = 0.08) of older age (Table 1).

Five participants in each dressing group were operated on. Operations were done at days 3, 5, 8 (n = 2), 9 (n = 2), 10,16,17,19, and 22 (reoperation/second surgery in the same patient) after injury. Of the 10 patients undergoing surgery 8 suffered from flame burns and 2 from scalds. One patient in the porcine xenograft group had the wounds debrided with hydro surgery (Versajet®) and left for secondary healing, all others were operated with excision and split-thickness skin grafting.

One case of erysipelas receiving antibiotics was reported in the porcine xenograft group, no other adverse events were reported in this trial.

Comparing the porcine xenograft and the BsC groups the burn distribution was similar (trunk 11 vs 13, upper extremity 7 vs 8, and lower extremity 8 vs 6).

3.1. *Primary outcome*

3.1.1. *Healing time*

Only participants with weekly healing assessment (7 ± 2 days) were included in the analysis of healing time. Eleven participants from the BsC group and 7 from the porcine xenograft group fulfilled this criterion, meaning that 2 from the BsC group and 4 from the porcine xenograft group were excluded from this analysis.

The time to ≥95% healing were similar between groups (p = 0.716). Median time in the porcine xenograft group was 19 (*range* 12–35) days, and in the BsC group 18 (*range* 10–35) days. The 3 patients with healing times more than 1 month (1 patient

with 33 days and 2 patients with 35 days each) had been operated, this indicates that those burns were deep dermal or full thickness.

We found no significant difference in healing time between groups when excluding the 7 participants undergoing surgery (p = 0.409). Median time in the porcine xenograft group for spontaneously healed participants was 18 (range 17–20) days, and in the BsC group 17 (range 10–24) days.

Of the 7 participants that were excised 3 came from the BsC group and 4 from the porcine xenograft group. We found no significant difference in healing times between the groups when including only excised participants (p = 0.372). Median time in the porcine xenograft group for excised participants was 21 (range 12–35) days, and in the BsC group 33 (range 20–35) days.

3.2. Secondary outcomes

3.2.1. Burn wound infection

Both groups were similar in wound infection rate, antibiotic use, and C-reactive protein levels (Table 2). All in the porcine xenograft group and 11/13 in the BsC group showed two or more signs of wound infection whereas only eight in each group were prescribed antibiotics for this purpose. The highest C-reactive protein levels in the porcine xenograft group was seen on days 6–8 whilst in the BsC group, it was on days 3–5.

The most common bacteria found in wound swabs was *Staphylococcus aureus,* which was found in 33% of all positive swabs (42/127), followed by *Staphylococcus epidermis* in 15 samples (12%). In Table 3 all bacterial types found are displayed. Study dressings were applied under sterile conditions in six cases in the porcine xenograft group and seven in the BsC group, in the remaining cases study dressings were applied under clean conditions.

3.2.2. Pain

Pain scores at rest and activity were similar between groups at all-time points. No analysis was possible for NRS at dressing changes due to large numbers of missing data, because most patients were sedated for the procedure. The highest NRS scores were noted on the second visit (approximately 5–8 days after injury) in both dressing groups. Median scores and range (min-max) at different time points can be seen in Figs. 1 and 2.

3.2.3. Impact on everyday life

Regarding impact on everyday life scores no differences were found. The highest impact on everyday life scores was noted on the second visit (approximately 5–8 days after injury) in both dressing groups (Table 4). Most common cause for dressings having an impact on everyday life was limitation of movement, which was noted in 13 of the participants (porcine xenograft = 6, BsC = 7).

3.2.4. Cost

At the time of the study, the cost for the porcine xenograft was $0.26/cm^2 compared with $0.15/cm^2 for the biosynthetic cellulose. When comparing the amount of dressings (in square centimeters) used in each group per TBSA % burned (208 cm^2 versus 286 cm^2 for porcine xenograft and BsC groups respectively) and multiplying this with the cost per square centimeter for the dressings no significant difference in cost between the two groups was found (non-parametric test p = 0.115, t-test p = 0.155).

3.2.5. Burn scar outcome at the six-month follow-up

As for the burn scar outcome, the area given the highest scar score was chosen for analysis as seen in previous studies [23–25].

A total of 19 participants visited the centers for the six-month follow-up, nine from the porcine xenograft group and 10 from the BsC group. We found no difference between the two dressing groups in any of the POSAS items or the total score. Median Observer POSAS total score for the six months follow-up was 21 (11–31) in the porcine xenograft group and 22 (8–29) in the BsC group (p = 1.0). All item scores and p-values can be seen in Table 5.

Of the 19 participants at the six month follow-up, 15 chose to fill in the patient part of the scale, eight from the porcine xenograft group and seven from the BsC group. Median patients' total scores for the six months follow up was 38 (21–55) in the porcine xenograft group and 21 (13–54) in the BsC group. All item scores given by the patients and p-values can be seen in Table 5.

3.2.6. Burn scar outcome at the 12 month follow-up

A total of 15 participants visited the centers for the 12 month follow-up, seven from the porcine xenograft group and eight from the BsC group. We found no difference between the two dressing groups in any of the POSAS items or the total Observer

Table 2 – Secondary outcomes by dressing treatment.

	Porcine Xenograft (n = 11)	BsC (n = 13)	p value
Patients with signs of infection	11	11	0.482
Patients with positive wound swabs	11	12	1.0
Antibiotic use	8	8	0.679
C-reactive protein concentration			
Day 0–2 (after injury)	71 (0–320)	13 (0–185)	0.171
Day 3–5	137 (35–360)	130 (5–333)	0.557
Day 6–8	180 (33–333)	73 (13–332)	0.099
Duration of hospital stay, days	14 (2–28)	4 (0–40)	0.331

Data are number, or median (10–90 centiles).

Table 3 – Number of microbial swabs with bacterial growth by dressing group.

	Porcine Xenograft swabs/patients	BsC swabs/patients
Acinetobacter	0	2/1
Bacillus species	8/4	4/3
Beta-hemolytic streptococci (Group G)	5/2	2/1
Candida albicans	0	1/1
Corynebacterium	0	1/1
Enterobacter cloacae or aerogenes	0	13/2
Enterococcus faecalis or casseliflavus	6/3	3/2
Klebsiella pneumonia	1/1	0
Methicillin-resistant Staphylococcus aureus	0	3/1
Pseudomonas aeruginosa	1/1	2/1
Staphyloccocus aureus	19/5	23/8
Staphylococcus capitis	0	4/2
Staphyloccocus epidermis	5/6	10/6
Staphyloccocus hominis (KNS)	5/3	3/3
Staphylococcus lugdunensis	2/1	0
Staphylococcus simulans	3/1	0
Streptococococcus agalactiae	2/2	1/1

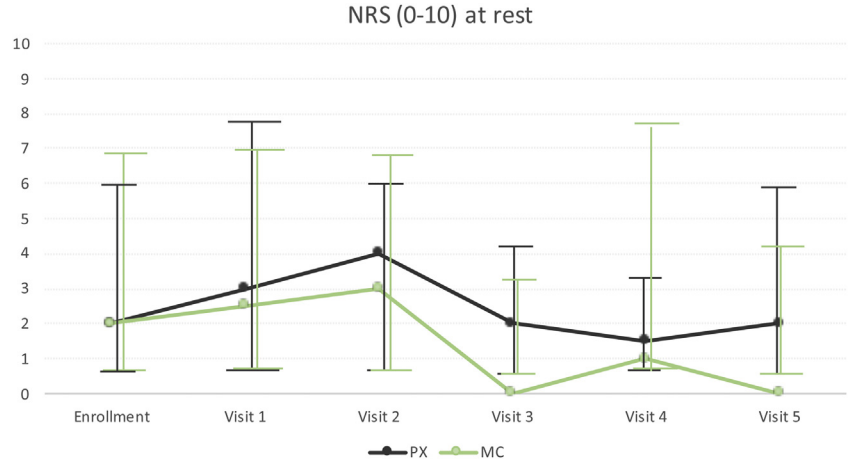

Fig. 1 – Median and min–max NRS score at rest for visit 0–5 for the porcine xenograft and BsC group.

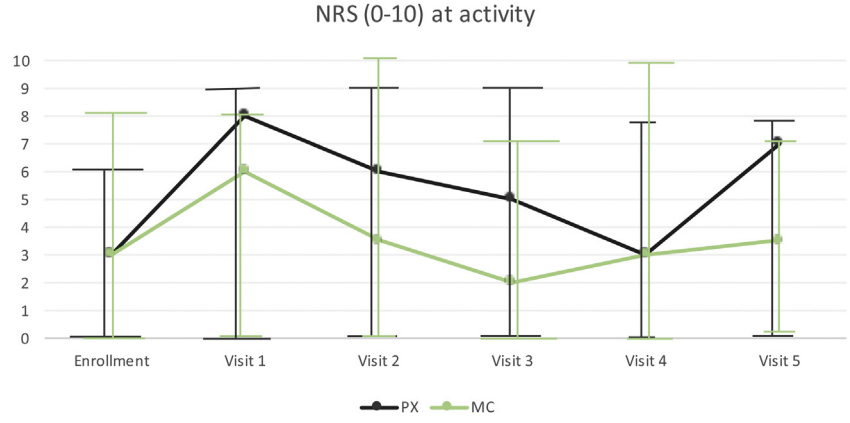

Fig. 2 – Median and min–max NRS score at activity for visit 0–5 for the porcine xenograft and BsC group.

score. Median Observer POSAS Total score for the 12 month follow-up was 20 (13–40) in the porcine xenograft group and 19 (11–25) in the BsC group ($p = 0.451$). All item scores and p-values can be seen in Table 5.

Of the 15 participants at the 12 month follow-up, 12 chose to fill in the patient part of the scale, six from the porcine xenograft group and six from the BsC group. We found no difference in the total Patient score ($p = 0.39$). Median patients'

Table 4 – Impact on everyday life scores (0–10) by visit and dressing group.

	Porcine Xenograft	BsC	p Value
Visit 1	3.5 (0–10)	4 (0–6)	0.632
Visit 2	5.0 (0–10)	5 (0–7)	0.573
Visit 3	4.0 (3–5)	2 (0–5)	0.237
Visit 4*	3.0 (1–8)	0 (0–0)	0.137
Visit 5*	2.5 (0–5)	0 (0–0)	0.480

Table 5 – POSAS scores at 6 and 12 months, all items displayed by dressing groups.

	Porcine Xenograft 6 months	BsC	p Value	Porcine Xenograft 12 months	BsC	p Value
Patient part						
Pain	1 (1–5)	3 (1–8)	0.501	2 (1–6)	3 (1–8)	0.669
Itching	4 (1–9)	4 (2–9)	0.265	5 (3–9)	4 (2–10)	0.870
Colour	9 (6–10)	6 (3–7)	0.075	9 (6–10)	4 (2–10)	0.121
Stiffness	7 (4–9)	3 (1–8)	0.220	5 (3–9)	5 (2–7)	0.573
Thickness	2 (6–9)	3 (1–8)	0.315	9 (5–10)	3 (2–8)	0.048
Relief	5 (3–9)	3 (1–9)	0.268	9 (6–10)	5 (1–8)	0.050
Overall opinion	7 (3–10)	3 (2–7)	0.161	8 (6–10)	6 (1–10)	0.462
	6 months			12 months		
Observer part						
Vascularity	3 (1–5)	4 (2–4)	0.502	3 (2–6)	3 (2–3)	0.336
Pigmentation	4 (3–6)	4 (1–7)	0.591	4 (3–5)	4 (2–6)	1.0
Thickness	2 (1–4)	3 (1–5)	0.835	2 (2–8)	3 (2–4)	0.952
Relief	2 (1–3)	2 (1–3)	0.796	2 (2–8)	3 (1–4)	0.432
Pliability	2 (2–6)	3 (1–4)	0.676	2 (2–8)	3 (2–4)	0.856
Surface area	6 (2–7)	4 (1–9)	0.837	4 (2–8)	3 (2–7)	0.343

Data are median (10–90 centiles).

total scores for the 12 month follow-up was 45 (31–61) in the porcine xenograft group and 33 (11–55) in the BsC group. The porcine xenograft group scored higher on the items thickness and relief ($p = 0.048$ and $p = 0.050$), although close to the significance cut off. All item scores given by the patients and p-values can be seen in Table 5.

3.3. *Loss to follow-up*

Five patients did not return for the six month scar follow-up, two from the porcine xenograft group and three from the BsC group. For the 12 month follow-up eight participants did not return, four from each dressing group.

4. Discussion

As far as we know, this is the first time a porcine xenograft has been compared to biosynthetic cellulose in patients with partial-thickness burns. The results showed that no difference in healing time (primary outcome measure) between the two study groups/dressings.

The number of studies evaluating the use of porcine xenograft in partial-thickness burns are limited. In 1989 Healy et al. compared EZ-derm (the porcine xenograft used in this study) with the paraffin gauze Jelonet in 32 patients with TBSA % less than 10% and found no significant difference between dressings regarding healing times, number of operations, or wound colonization. Healing times reported were 12.9 days for the porcine xenograft and 12.5 days for the Jelonet [26].

In 2011 Zajicek et al. compared the porcine xenograft Xe-Derma with Askina THINSite a synthetic hydrogel in scalded children with a mean TBSA of 7–10% and found no significant difference regarding healing times, conversion to a deeper burn, or infection rates. The porcine xenograft underwent significantly less dressing changes than the hydrogel dressing. Healing times were 8 (IQR 5–10) days for the porcine xenograft and 7 (3–10) for the hydrogel [27].

In 2019 Karlsson et al. reported results of a RCT comparing EZ-derm® with a silver foam dressing in partial-thickness burns in children with a median TBSA % of 5 (10–90th centiles 3–11). The porcine xenograft showed longer healing times than the silver foam and more time consuming dressing changes. We found no differences in pain, duration of hospital stay, or infection. Reported healing times for porcine xenografts in this study was median 15 (9–29) days compared to the silver foam with 9 (7–23) days [16].

Regarding the BsC, this dressing is more novel, limiting the number of (any) studies on burns published. Aboelnaga et al. reported in 2018 results of an RCT where Epiprotect® (the BsC used in this study) was compared with silver sulfadiazine in partial-thickness burns with a median TBSA % of 9% (IQR 5.5–12.5), they found no significant difference in healing times, number of operations, duration of hospital stay, or infection rates. Pain and number of dressing changes were lower in the BsC group. Similar to our study a median healing time of 18.0 (IQR 14.0–23.0) days was reported for the BsC and 16.5 (IQR 14.5–32.5) days for the silver sulfadizine [28].

In 2020 the same type of BsC was evaluated by Shanks et al. in scalded children under the age of 5 years with burns of a median of 4.5% TBSA (min–max 2%–12%). Shanks reported median healing times of 13 days for superficial partial-thickness burns (min–max 8–21 days); 14 days for mid partial-thickness burns (min–max 9–26 days); and 24 days for deep partial-thickness burns (min–max 21–26 days). The median healing time for skin grafted patients was 28 days (min –max 21–48 days) [29].

4.1. *Healing time*

The healing times reported in this study are similar to other studies of partial-thickness burns of similar extent with the same dressings used (as seen above).

A Cochrane report from 2013 on partial-thickness burns dressings summarizes healing results for eight dressing types (hydrocolloids; polyurethane films; hydrogels; silicon-coated nylon; biosynthetic skin substitutes; antimicrobials, fibers, and wound dressing pads) and all dressings types were associated with similar or shorter healing times than what was seen in this study [30].

As the study population included patients who were operated on with excision and skin grafting, it is evident that patients who had apparently deep burns and considered not fitting for spontaneous healing were considered for surgery, however those patients were kept in the study and data about healing time and follow-up was presented.

The average number of dressing changes is 1–2 times per week in this study, a higher frequency of dressing changes can result in a more accurate (earlier) date for the actual time point of healing, factors not accounted for in this discussion.

4.2. *Secondary outcomes*

4.2.1. *Inflammatory response and wound infection*

A total of 16 participants (67%) were treated with antibiotics for suspected wound infections and a total of 22 patients had signs of infection documented (92%). These numbers are higher than normally reported for this kind of burns [17,31,32]. This could possibly be related to the non-use of prophylactic antibiotics, generous wound infection criteria, high surveillance rate of C-reactive protein levels, and routine microbial swabbing of wounds.

The trend in C-reactive protein differed between groups as the BsC group had a peak in C-reactive protein after five days whilst the porcine xenograft group had a later peak. Two similar studies on partial-thickness burns but in children did not show the same C-reactive protein trend for the porcine xenograft treated group, but these burns were mainly scalds and the median TBSA lower (5–7% compared to 12% here) possibly affecting the C-reactive protein response [16,20].

4.2.2. *Pain and impact on daily life activities*

Regarding pain scores the BsC group had a lower median score at rest and during activity at all time-points, even though not significantly so. Figs. 1 and 2 show a peak in pain at visits one and two, and median pain scores well above three on the NRS scale at activity reflecting insufficient pain relief for the participants (seen also in other studies) [33]. Similar (or lower) pain scores have been reported for other burns dressings [33–36] but as burn depth and extent differ significantly, conclusions cannot be drawn. As the impact on everyday life scale was created by the authors themselves, no conclusion can be drawn other than that more than 50% (13/24) of the patients complained of the study dressings' limitation of mobility, an experience confirmed by clinicians at the burn centers and seen with other types of dressings also [37].

4.2.3. *Length of stay in the hospital*

We found no significant difference in hospital stay between the two groups. Since the trial sites are the only two national centers for burn care in Sweden the day for discharging the patient may differ from the actual day that the patients were no longer receiving in-hospital care, depending on logistical factors, such as long travelling distances, leaving any interpretation or comparison with other studies likely to be biased, which makes it difficult to interpret this finding.

4.2.4. *Cost*

The analysis on cost (dressing material used) did not show a significant difference even though the cost per square centimeter was lower for the BsC. This might be related to more dressings being used in the BsC group as only one size is available (more dressing material was therefore disposed of). Approximately 286 cm^2 of BsC was used per TBSA treated and 208 cm^2 for the porcine xenograft.

Regarding secondary dressings, the polyethylene net was used in 3 participants in the porcine xenograft group and in the remaining 21 participants paraffin gauze was used. As mentioned in the method prices for these dressings were similar.

4.2.5. *Scar follow-up*

The analysis of the participants' own opinion on the scars tells us that seven of out 15 participants felt pain in the scar six months after injury and eleven suffered from pruritus in the scar. At 12 months, six out of 12 suffered from pain and 10 out of 12 from pruritus, reflecting a very troublesome situation for this patient group that has also been reported in previous studies in similar patient populations. Studies show that burn patients can suffer from pruritus up to 30 years after injury [38,39]. The dressing groups scored similar in all POSAS items at six and 12 months regarding pain, itching, pigmentation, and stiffness, but the BsC group scored significantly lower in thickness and close to significantly lower in relief at the 12 month follow-up (however not confirmed by the Observer). A similar study on silver sulfadizine and Flaminal®, but in smaller burns, showed similar or lower POSAS results for the six and 12 month follow-up than the BsC group, except for the overall opinion. Patients scored a median of three in silver sulfadizine group and median of two in the Flaminal® - group compared to the median of eight in the porcine xenograft group and six in the BsC group, indicating fewer patients were satisfied in our study. As the number of observations were small in our study (six patients from the porcine xenograft group and six from the BsC group) conclusions and interpretations are unreliable.

Looking at Observer scores they were similar between six and 12 months and also between groups on both occasions. As the patient return rate was low between six and 12 months (participants scored on both occasions) no analysis could be

done on improvements over time. Interestingly, when looking at which scar was given the highest score (if more than one scar was evaluated) patients and observers agreed on which was the "worst" scar in all cases without being exposed to the scar evaluation from the other part. The Observer scores were similar to those given in the study on silver sulfadizine and Flaminal® mentioned above.

4.2.6. *Limitations of the study*

The number of patients was limited. The sample size was calculated to 26 patients, but as two participants chose to withdraw, the final number of included patients was 24 of which 18 could be included in the healing analysis. In retrospect, we think that future sample size calculations should to a greater extent take into account the great variability that may exist, and the loss to follow-up that hampered the analysis of long-term outcome in the present study. The depth of the burns as well as time to healing were evaluated by multiple burn surgeons, which entails a loss of standardization. Moreover, because the dressings were evident on the wounds at the time of dressing change and wound evaluation, blinding was not possible which may have introduced bias to the study. On the other hand, doing a blind evaluation of different dressings that are different in appearance for the observer is not possible. Also a gender imbalance (91.7% male) needs to be added to the limitations of the study.

5. Conclusion

Two different dressings (porcine skin and biosynthetic cellulose) for burns that were evaluated as partial thickness burns at admission were compared. We found no differences in rates of healing, infection, pain, impact on everyday life, length of hospital stay, need for operations, or total scar scores between dressings. After one year, patients with porcine xenograft dressings scored their scars worse on the items thickness and relief, but this was not confirmed by the observer. The power of these conclusions is, however, hampered by the small number of patients in this study.

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Conflict of interest

The author Folke Sjöberg reports stock ownership in the manufacturing company S2Medical AB. The other authors declare no conflict of interest.

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