


The impact of incisional negative pressure wound therapy on scar quality and patient-reported outcomes: A within-patient-controlled, randomised trial

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Abstract

Literature provides a moderate level of evidence for the beneficial effects of incisional negative pressure wound therapy (iNPWT) on scar quality. The purpose of this study was to establish if iNPWT results in improved scar outcomes in comparison to the standard of care. Therefore, a within-patient randomised controlled, open-label trial was conducted in transgender men undergoing gender-affirming mastectomies. A unilateral side was randomised to receive iNPWT (PICO™, Smith&Nephew) without suction drains and contrastingly the standard dressing (Steri-Strips™) with suction drain. Scar quality and questionnaires were bilaterally measured by means of objective assessments and patient-reported outcome measures (PROM) at 1, 3 and 12 months. Objective scar outcomes were scar *pliability* (Cutometer®), *colouration* (DSM-II) and *scar width* (3-D imaging). PROM outcomes were related to scars (POSAS and SCAR-Q) and body satisfaction (BODY-Q). From 85 included patients, 80 were included for analyses. No significant difference between treatments was seen in the quantitative outcomes of *scar pliability*, *colour*, and *width*. For qualitative scar outcomes, several significant findings for iNPWT were found for several subscales of the POSAS, SCAR-Q, and BODY-Q. These effects could not be substantiated with linear mixed-model regression, signifying no statically more favourable outcome for either treatment option. In conclusion, this study demonstrated that some PROM outcomes were more favourable for the iNPWT compared to standard treatment. In contrast, the quantitative outcomes showed no beneficial effects of iNPWT on scar outcomes. This suggests that iNPWT is of little benefit as a scar-improving therapy.

KEYWORDS

gender reassignment surgery, mastectomy, negative pressure wound therapy, patient-reported outcome measure, scar, transgender, wound healing

TRIAL REGISTRATION

NTR7412.

1 | BACKGROUND

On average, surgeons create a total of 200 million incisions annually.¹ All scars are at risk to develop into pathological scars, such as hypertrophic or keloid scars. Pathological scars can lead to different issues and complaints such as pain, itching, aesthetic complaints and functional disabilities or disfigurements.²⁻⁴ These types of scars can induce the need for long-term rehabilitation, revision surgery or other invasive therapies.⁵ Pathological scar development is especially prevalent in chest masculinizing surgery in transgender men, with reported hypertrophic scars in 8%–13.6% of individuals.^{6,7} To reduce complicated scar formation, some have suggested the use of incisional negative pressure wound therapy (iNPWT). Although recent studies have shown certain limitations of the use of iNPWT, the general consensus remains that iNPWT helps to reduce surgical site complications such as infections and dehiscence in non-contaminated surgery.⁸⁻¹⁰ Furthermore, several studies have reported beneficial effects of iNPWT on scar development.^{11,12} The underlying mechanism is hypothesized to be the reduction of lateral wound tension. Excessive lateral tension is generally considered to be a factor in pathological scar formation, and reduction of incisional tension has previously been shown to result in more favourable scar outcomes.¹³⁻¹⁶ Studies into the biomechanical properties of iNPWT demonstrated lateral tension reduction of the epidermis, fat, and muscle, supporting the hypothesis that negative pressure reduces sheer tension.^{12,17} Moreover, iNPWT was also shown to increase the overall incisional stress resistance in preclinical studies.^{11,18,19} In a recent systematic review by Zwanenburg et al., the conclusion was that there is a moderate level of evidence for clinically positive effects of iNPWT on scar outcomes in non-contaminated surgery.²⁰ Unfortunately, the literature on scars and iNPWT relies heavily on studies with small sample sizes, a short length of follow-up, non-blinded evaluations, and heterogeneous outcomes for measuring scar quality. Due to iNPWT being used for a plethora of indications, it is important to establish the actual benefits. Therefore, the purpose of this study was to establish if iNPWT results in improved scar outcomes in comparison to the standard of care, by means of both objective scar evaluations and patient-reported outcome measures.

2 | METHOD

2.1 | Study design and participants

This was a prospective, open-label, within-patient randomised controlled trial (left–right comparison) performed at the Amsterdam UMC, location VUmc between August 2018 and August 2020. A within-patient controlled set-up was chosen to avoid the effects of inter-patient variability with regard to scar formation and outcome evaluation.

The primary end-point of the study, which was wound healing complications within 3 months postoperatively, has been reported previously.¹⁰ This study showed that the application of iNPWT versus conventional wound dressings and surgical drains, did not decrease postoperative complications (hematoma, dehiscence and infection), but actually increase the likeliness and severity of seroma formation. The participants did report increased comfort and pain relief on the iNPWT-applied site during the first 6 days after surgery. In this article, the secondary outcomes are presented. The secondary outcomes of this study were the scar elasticity (Cutometer[®]), colouration (DermaSpectrometer[®]), 3-D assisted scar width measurements (VECTRA 3D), POSAS 2.0 Patient and Observer Scale, SCAR-Q (scar symptom, appearance, and psychosocial scale) and BODY-Q (chest and nipple modules). All these outcomes are elaborated on in the following paragraphs. Transgender men who were scheduled to undergo a gender-affirming mastectomy were considered for participation. All participants were of age (>18 years), had been diagnosed with Gender Dysphoria according to the DSM criteria, and were being treated according to the Standards of Care by the World Professional Association for Transgender Health.²¹ Before entry into the study, all participants signed an informed consent form, with an optional “use of photographs” form. Exclusion criteria included excessive smoking (>22 cigarettes a day) and having known comorbid medical conditions that may interfere with normal wound healing (i.e., diabetes, chronic corticosteroid use). For the final analysis, only patients were included who had either visited the outpatient clinic once for a scar assessment or who at least responded to the online questionnaires once.

2.2 | Study procedure

Patients were asked to participate in this study prior to undergoing a bilateral gender-affirming mastectomy. Study visits were at screening (pre-surgery), day 0 (day of surgery), day 7, 30, 90 and day 365 post-surgery. Online questionnaires (*Castor EDC, Amsterdam, the Netherlands*) were sent out at screening, at 30, 90 and 365 days. A graph for this study design is presented in Figure 1. Scar and patient-reported outcomes were measured on days 30, 90 and 365.

2.3 | Randomization and blinding

One chest half was randomly assigned to receive iNPWT versus the contralateral control side. An online randomization tool (*Castor EDC, Amsterdam, the Netherlands*) was used for the within-patient allocation. Randomization of iNPWT was disclosed in the re-sealed iNPWT package and revealed to the operation team at the time of dressing application after surgery. This study was set up as an open-label study.

2.4 | Study intervention

Based on skin quality, breast size and ptosis of the breast, the most appropriate type of mastectomy (double incision mastectomy or

[periareolar] concentric circular mastectomy) was decided on before surgery by the gender surgeon.²² Vicryl 3.0 (deep dermal, interrupted) and Monocryl 4.0 (subcuticular, continuous) (Ethicon, Johnson & Johnson, Edinburgh, UK) were used to close the dermis and epidermis, respectively. After randomization, the incision on the standard of care (SOC) side was covered with Steri-Strips™ (3 M Health Care, St. Paul, MN, USA). A high vacuum (down to -600 mmHg) wound drainage system was inserted into the wound cavity (van Straten, Medinorm, Spiessen-Elversberg, Germany) and fastened to the outside skin with a single suture. The drain removal criteria were (1) no exudate was seen for 12 hours or (2) when less than 30 cc exudate per 24 hours was observed. As a study intervention (iNPWT), we used the PICO™ 5.0 (Smith & Nephew Medical Limited, Hull, United Kingdom), a portable, non-canister, single-use (up to 7 days) system that delivered -80 mmHg at the wound surface. Specific considerations were given in covering the entire surface of the (subdermal resection) wound and (sutured) incision. A transparent dressing of 20 cm by 20 cm was provided with the iNPWT and sufficed in all patients to cover up the entire wound bed. In accordance with the clinical guidelines provided by Smith & Nephew, no surgical drain was placed on the iNPWT allocated side.²³ Patients were required to wear a thoracic pressure garment 24 hours a day for up to 6 weeks after surgery.

3 | OUTCOMES

3.1 | Quantitative scar measurements

The main outcome of this study was quantitative scar quality at 1-year follow-up, by means of the Cutometer® (Courage & Khazaka GmbH, Cologne, Germany), the DermaSpectrometer® (DSM-II) (Cortex Technology, Hadsund, Denmark), and scar width measurements. The Cutometer® is a device that allows for a validated evaluation of scar elasticity.²⁴ The results are presented as a ratio between the scar tissue and adjacent unaffected skin values. The DSM-II® is a validated instrument that allows for measurements of vascularization (erythema) and pigmentation (melanin) by a narrow band simple reflectance meter.^{24,25} The outcomes of the DSM-II® are presented as the absolute difference in erythema and melanin between the scar and the unaffected skin values, wherein larger outcomes signified a larger difference. Scar width was measured on three-dimensional images taken at 1, 3 and 12 months follow-up (VECTRA 3D, Canfield, Parsippany, USA) at pre-defined locations (Figure 2) with a precision of 0.1 mm. For linear scars, elasticity (Cutometer®), colour (DSM-II) and scar width, three points were measured at 1 cm distances from the scar borders and the midpoint. For circular periareolar scars, two measurements were made at 12 o'clock and 6 o'clock. Importantly, specific consideration was given to

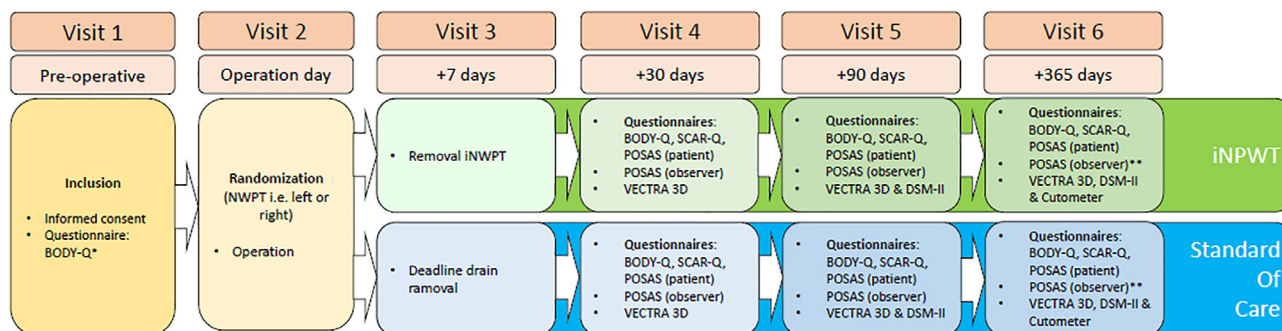


FIGURE 1 Study procedure. *Modules: Chest and Nipple, **two single-blinded assessments; Abbreviations: DSM; DermaSpectrometer; iNPWT, incisional negative pressure wound therapy [Color figure can be viewed at wileyonlinelibrary.com]

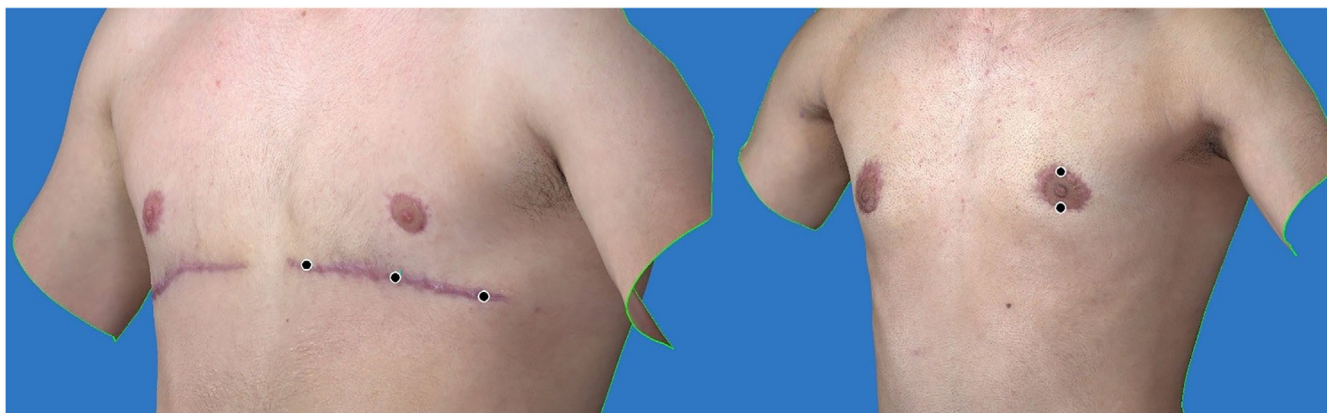


FIGURE 2 Depiction of the measuring points (inframammary mastectomy (left); lateral, central and medial - concentric circular (right); cranial and caudal) for the Cutometer, DSM-II and scar width [Color figure can be viewed at wileyonlinelibrary.com]

first performing the colour measurements, as the suction probe of the Cutometer® might increase local perfusion and, therefore, erythema outcomes.

3.2 | Observer reported outcome measure

The observer-reported outcomes were collected using the Observer Scar Assessment scale (POSAS 2.0). The POSAS Observer scale is a reliable and validated scar assessment scale.^{24,26} The six parameters of the Observer Scale are (1) *vascularization*, (2) *pigmentation*, (3) *thickness*, (4) *relief*, (5) *pliability* and (6) *surface area*. The observer assessment was performed at study visits at 30, 90 and 365 days. The summed outcome range can be between 6 and 60, with 6 being “normal skin” and 60 being “the worst imaginable scar”. Scar assessments and questionnaires were taken twice at each time point, once for each side. Due to initial limitations in staff availability, the observer assessments at 30 and 90 days were non-blinded and performed by a single dedicated physician (F.T). Specific consideration and planning were given to the final assessment at 365 days, where two blinded clinical staff members performed the observer assessment. The blinded clinical staff members at the 1-year follow-up were selected on the basis of having existing hands-on experience with POSAS Observer scale assessments. The outcomes of this final assessment are presented as a mean value of the two observers.

3.3 | Patient-reported outcome measures

The patient scale of the POSAS, SCAR-Q and BODY-Q were used to establish patient-reported outcomes. Scar questionnaires were taken twice at each time point, once for each side. The patient scales were administered as online questionnaires on days 30, 90 and 365. Similar to the observer scale, the POSAS–Patient scale exists of six parameters (1) *pain*, (2) *itching*, (3) *colour*, (4) *stiffness*, (5) *thickness* and (6) *surface irregularity*. Responses were gathered into scores ranging from 1 to 10 for each parameter. For both scales, the summed outcome range can be between 6 and 60, with 6 being “normal skin” and 60 being “the worst imaginable scar”. Secondly, the SCAR-Q was used. This is a patient-reported outcome scale that has three separate domains including *scar symptoms*, *appearance* and *psychosocial impact*. A sum conversion allowed for an outcome ranging from 0 (worst) to 100 (best) for each domain. The *symptom* and *appearance* domains were taken bilaterally, whereas the *psychosocial* domain was taken once at each follow-up moment. Lastly, the BODY-Q (modules *chest* and *nipple*) was administered bilaterally at screening and the above-mentioned time points. This questionnaire focused on the (dis)contentment with the chest and nipples.²⁷ Similar to the SCAR-Q, the sum outcomes were converted to a 0 (worst) to 100 (best) outcome.^{27,28}

3.4 | Sample size and statistical analysis

The sample size was a priori calculated based on the primary endpoint; the effect on wound healing complications.¹⁰ Therefore, effect sizes

and mean differences for each outcome were presented in the results to allow for post hoc analysis of power for each individual outcome. Descriptive statistics were used to describe demographics and baseline data. Normally distributed data were presented as means and standard deviations. Non-normally distributed and ordinal data were presented as medians with interquartile range 1–3. Outcomes of intervention and control sides were compared using paired-tests for normally distributed data and the Wilcoxon signed-rank test for non-normally distributed data. Effect sizes for normally distributed variables were presented as Cohen's *d* with a 95% confidence interval. The effect size for non-normally distributed variables is presented as the mean difference between the intervention and standard of care. Furthermore, a linear mixed-effect regression was performed for scar width, the POSAS–Observer, and Patient scale and the separate SCAR-Q and the CHEST-Q modules. Furthermore, the intraclass correlation coefficient (icc) for the blinded POSAS assessments at 12 months was calculated. An icc value under 0.2 was considered as slight agreement; 0.21–0.40 as fair; 0.41–0.60 as moderate; 0.61–0.80 as substantial; 0.81–1.00 as almost perfect agreement.²⁹ A *p*-value of <.05 was considered to be statistically significant. The statistical analyses were performed in spss (version 26.0) and *r* (version 3.6.3).

3.5 | Ethical issues

The Ethics Board for Research of the VU Medical Centre in Amsterdam approved this study, registered under NL64838.029.81. The study is registered as NTR7412 in the Netherlands National Trial Register (NTR). This study was performed in accordance with the Declaration of Helsinki, guidelines for Good Clinical Practice, and the CONSORT statement for reporting within-person randomised trials.³⁰

4 | RESULTS

4.1 | Patient demographics

In total, 85 patients were included in this study. Follow-up moments were between August 2019 and August 2020. Inclusion and surgery took place between August 2018 and August 2019. See Appendix A for the flow chart on the loss of follow-up. Patients received both the SOC and iNPWT treatment for either side of the chest. A total of 80 participants completed the primary study outcomes measures (on scar quality and patient-reported outcomes) and were included for analysis. The patient demographics are presented in Table 1. The median age of the participants was 21 years (range 18–63). A total of 18 patients (22.5%) were active smokers at the time of inclusion. None of the patients declared to have experienced any problematic scarring previous to surgery (e.g., hypertrophy and/or keloid). Most of the included patients were Caucasian (87.5%). A total of 65 inframammary mastectomies (81.3%) and 15 concentric circular mastectomies (18.7%) were performed.

4.2 | Quantitative scar assessment

On both sides, the Cutometer[®] showed an overall decreased pliability of the scar tissue in comparison to the unaffected skin. The outcomes for SOC and iNPWT showed no significant differences for any of the Cutometer[®] subdomains at any follow-up point. Similarly, for the DSM-II, no significant differences were seen in the erythema and melanin outcomes between the two chest halves. Levels of significance and effect sizes including their respective confidence intervals are presented in Tables 2 and 3. Scar width increased especially between one and three months, after which it stabilised up to the last visit. Furthermore, none of the scar locations showed

a significant difference between the intervention or SOC side at any of the, respectively, three, and two landmarks. Scar width for each separate landmark is presented in Figure 3. With regard to the overall effect across all follow-up moments, the linear mixed-effect regression for scar width showed no significant difference in favour of either treatment option.

4.3 | Qualitative scar assessment

4.3.1 | Posas – Observer scale

For the observer scale, the follow-up rates were, respectively, 95% (1 month), 92.5% (3 months) and 92.5% (12 months). The outcomes of the patient scale are plotted in Figure 4 and the in-depth statistical analysis, including the level of significance and mean differences, are presented in Table S1. At 1 month follow-up, no significant differences were established between the two intervention groups. At 3 months, the *vascularity* ($p = .022$), the *total score* ($p = .003$), and *overall impression* ($p = .004$) were significantly in favour of the iNPWT side, albeit with small effect sizes. At the 12 months follow-up, when mean values were calculated from two blinded observers, no significant differences between iNPWT and SOC were seen. With regard to the overall effect across all follow-up moments, the linear mixed-effect regression for the observer scale showed equal scar quality for either treatment option. The mean icc for the six separate domains was 0.726 (sd 0.077), which on average is considered a substantial agreement between the two observers. The separate icc calculations are presented in Table S1

4.3.2 | POSAS – Patient Scale

The response rates for the Patient scale were, respectively, 98.8% (1 month), 88.8% (3 months) and 96.3% (12 months). The outcomes of the patient scale are plotted in Figure 4 and the in-depth statistical analysis, including the level of significance and mean differences, are presented in Table S1. At the first and second points of measurement, only the *thickness* of the scar was scored

TABLE 1 Demographic data

	N = 80 (median (range), mean (SD))
Age (years)	21.0 (18–63)
Height (m)	1.68 (1.49–1.83)
Weight (kg)	67 (13.8)
BMI (kg/m ²)	24.6 (4.3)
Smoking (%)	
No	52 (65%)
Yes, actively	18 (22.5%)
Stopped	10 (8%)
Hormone replacement therapy	75 (93.8%)
Self-declared history of pathological scar formation	0
Co-occurring physical diagnoses*	10 (8%)
Co-occurring psychiatric diagnoses*	30 (24%)
Ethnicity (%)	
Caucasian	70 (87.5%)
Other (mixed)	10 (12.5%)
Mastectomy method	
Inframammary mastectomy	65 (81.3%)
Concentric circular	15 (18.7%)

*In compliance with inclusion criteria.

TABLE 2 Skin elasticity as assessed by the Cutometer at 12 months post-surgery

Skin elasticity parameters*	12 months post-surgery N = 74			
	SOC mean (SD)	iNPWT mean (SD)	p-value**	Cohen's d (CI 95%)
Max skin extension (Uf)	0.83 (0.27)	0.82 (0.22)	0.651	−0.05 (−0.29–0.18)
Skin pliability (Ua)	0.81 (0.30)	0.82 (0.29)	0.831	0.025 (−0.21–0.26)
Elasticity (Ue)	0.81 (0.31)	0.77 (0.24)	0.267	−0.13 (−0.36–0.10)
Relaxation (Ur)	0.77 (0.32)	0.76 (0.25)	0.717	−0.043 (−0.28–0.19)
Visco-elasticity (Uv)	0.93 (0.29)	0.95 (0.32)	0.641	0.06 (−0.18–0.29)

*Data are presented as mean ratio of the respective scar elasticity versus normal uninjured skin.

**All parameters were normally distributed and tested with the paired samples T-test.

Abbreviations: CI, confidence interval; iNPWT, incisional negative pressure wound therapy; SD, standard deviation; SOC, standard of care.

TABLE 3 Scar colour and pigmentation assessment at 3- and 12-months post-surgery

DSM-II parameters*	3 months follow-up N = 74				12 months follow-up N = 74			
	SOC mean (SD)	iNPWT mean (SD)	Cohen'ss d (CI 95%)	p-value*	SOC mean (SD)	iNPWT mean (SD)	Cohen'ss d (CI 95%)	p-value*
Erythema	3.84 (5.99)	3.51 (6.56)	-0.099 (-0.330-0.133)	0.399	3.04 (2.11)	3.04 (2.03)	0.002 (-0.230-0.233)	0.989
Melanin	7.46 (10.84)	7.52 (10.00)	0.009 (-0.223-0.241)	0.937	6.25 (5.89)	6.57 (5.82)	0.060 (-0.172-0.292)	0.607

*Data are presented as the mean difference of the absolute values of the respective scar versus normal uninjured skin.

Note: All parameters were normally distributed and tested with the paired samples T-test.

Abbreviations: CI, confidence interval; iNPWT, incisional negative pressure wound therapy; SD, standard deviation, SOC, standard of care.

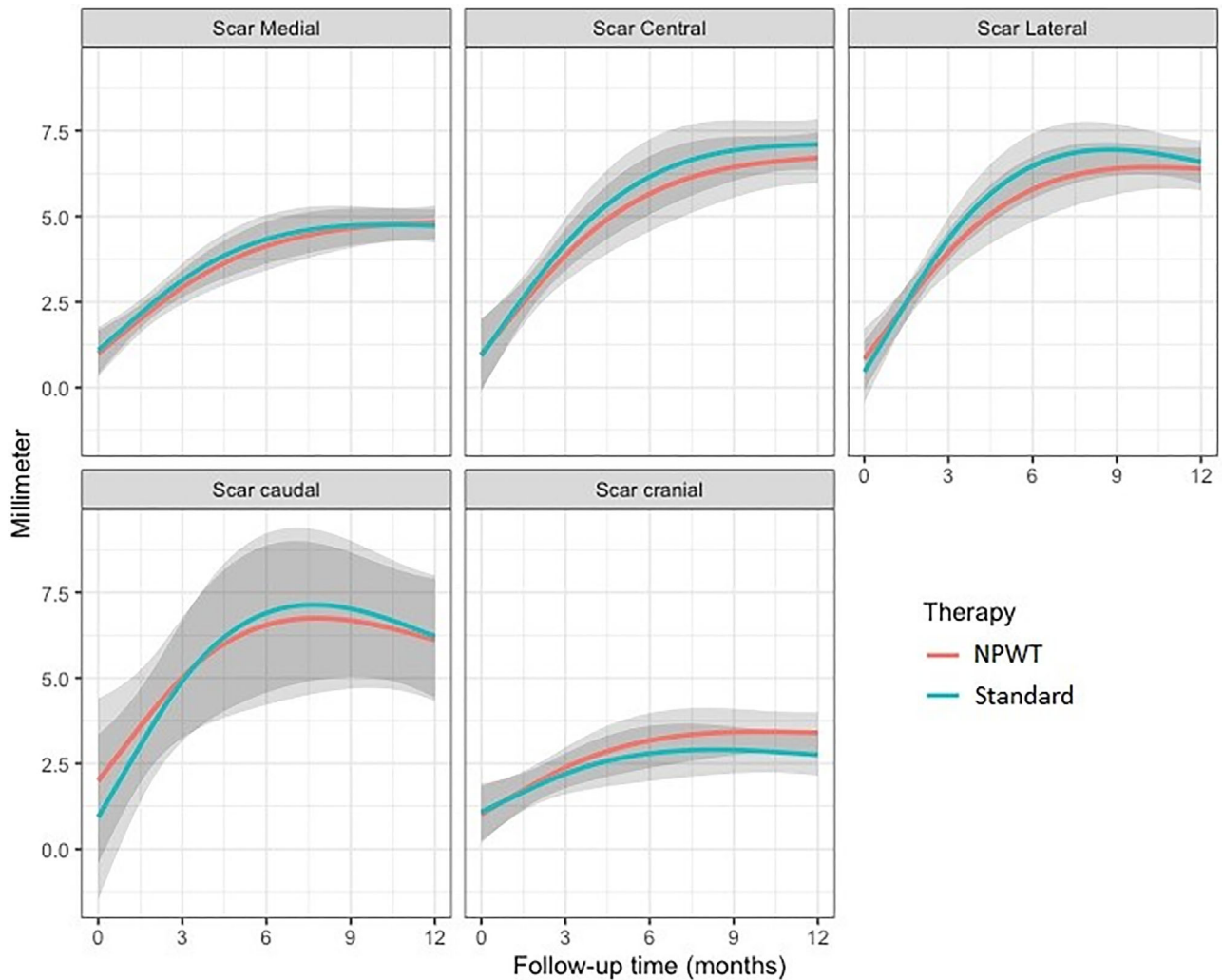


FIGURE 3 Effect plot of scar width outcomes over time for the linear and circular scars based on the linear mixed-effect model. Abbreviations: iNPWT: incisional negative pressure wound therapy; SOC, standard of care

significantly in favour of the iNPWT side (1 month; $p = .027$, 3 months; $p = .042$). At 12 months follow-up, *colour* ($p = .003$), *pliability* ($p < .001$), *thickness* ($p = .003$), *total score* ($p = .039$) and *overall opinion* ($p = .008$) were significantly in favour of the iNPWT side, albeit with small effect sizes. The mean differences in favour of iNPWT at 12-months ranged from 0.0068 to 0.1081 on the 10-point scale. With regard to the overall effect across all follow-up moments, the linear mixed-effect regression for the Patient

Scale showed no significant difference in favour of either treatment option.

4.3.3 | SCAR-Q

The SCAR-Q response rates were, respectively, 95% (1 month), 88.8% (3 months) and 96.3% (12 months). The outcomes of the SCAR-Q

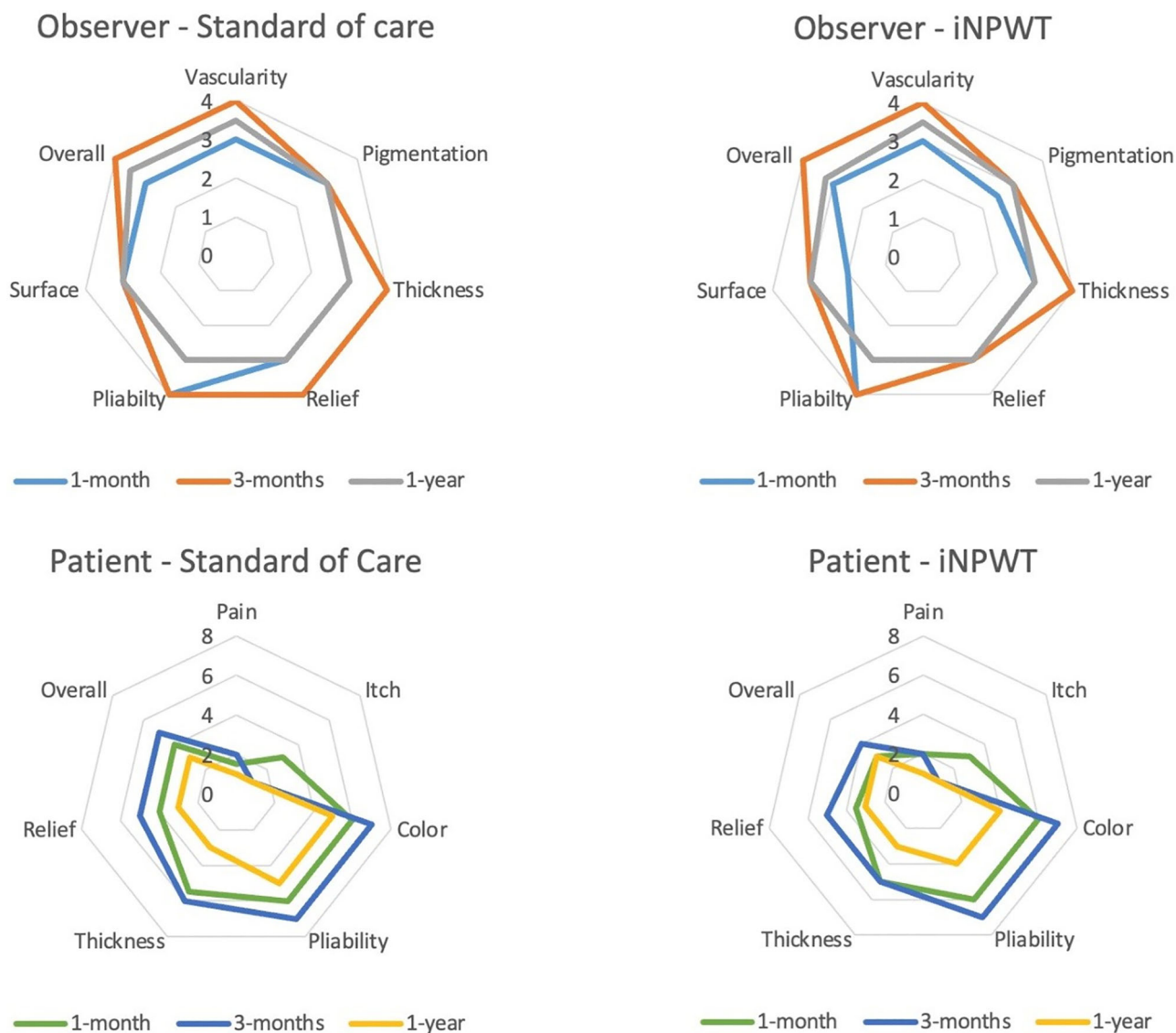


FIGURE 4 Radar plots for median outcomes for the POSAS—*Observer* and *Patient* scale during 1 month, 3 months and 1-year follow-up. Legend: 1; normal skin to 10; worst scar imaginable or very different from normal skin

modules are shown in Figure 5 and the in-depth statistical analysis, including the levels of significance and effect sizes, are presented in Table S2. At 1 month follow-up, patients reported significantly less impactful scar *symptoms* at the iNPWT side ($p = .006$). At 3 months, the *symptom scale* lost significance, but the *appearance scale* was found to be significantly in favour of the iNPWT side ($p = .045$). At the final measuring, only the *symptom scale* was reported to be better for the iNPWT side ($p = .003$). The overall score for the *appearance scale* decreased between 1 and 3 months, signifying a worsening, and remained at a similar level at 12 months. The *symptom scale* gradually increased over time, reflecting less experienced symptoms related to the scars. The median outcome of the *psychosocial scar scale* was most favourable at 1-month follow-up (100, 77–100), and decreased at 3 months (77, 69–100). At the final assessment, the psychosocial outcome remained identical to the 3 months outcome. With regard to the overall effect across all follow-up moments, the linear mixed-effect

regression for the SCAR-Q domains showed equal scar quality for either treatment option.

4.3.4 | BODY-Q

The response rate for these questionnaires were, respectively, 100% (pre-operative screening), 95% (1 months), 88.8% (3 months) and 96.3% (12 months). Satisfaction with the chest was improved after surgery and remained high, but was not significantly in favour of the SOC or iNPWT. The outcomes of the BODY-Q modules are shown in Figure 6 and the in-depth statistical analysis, including the levels of significance and effect sizes, are presented in Table S3. With regard to the overall effect across all follow-up moments, the linear mixed-effect regression for the BODY-Q domains showed no significant difference in favour of either treatment option.

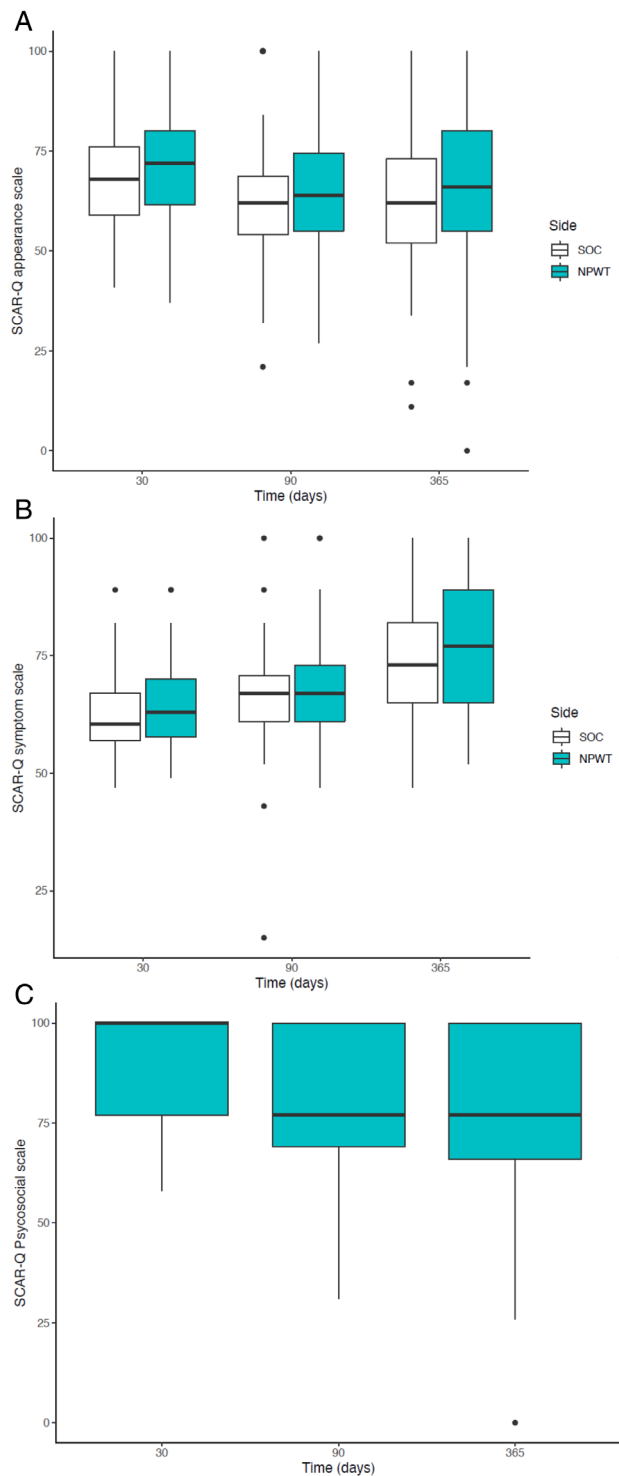


FIGURE 5 SCAR-Q outcomes for the *Appearance* (a), *Symptom* (b) and *Psychosocial* (c) scale. Abbreviations; NPWT, incisional negative pressure wound therapy; SOC, standard of care [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.com)]

5 | DISCUSSION

In this study, we assessed the influence of incisional negative pressure wound therapy (iNPWT) on scar development and patient satisfaction.

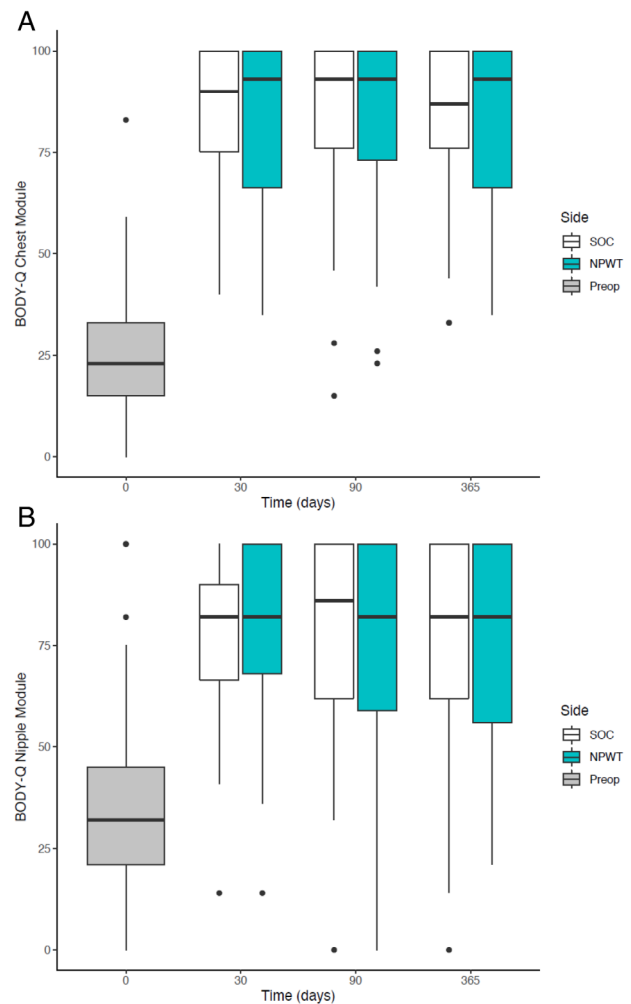


FIGURE 6 BODY-Q outcomes for the *Chest* (a) and *Nipple* (b) module. Abbreviations; iNPWT: incisional negative pressure wound therapy; SOC, standard of care [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.com)]

We performed a within-patient randomised controlled trial to test two equivalent incisions without confounding inter-person variables that could influence scar formation. Generally, the results of this study showed some small but significant differences in favour of iNPWT in patient-reported outcome measures. These outcomes could not be substantiated with quantitative measures and blinded observer assessments at 12-months follow-up. Furthermore, the linear mixed-effect regression analysis was unable to detect any persisting and continuous advantage of iNPWT across the whole 12-months follow-up period.

The quantitative measures showed no significant differences between treatments for skin elasticity at 12 months or erythema and melanin outcomes at 3 and 12 months. Tenaydin et al. is the only other known study to have used the Cutometer[®] to measure scar viscoelasticity in scars of iNPWT-treated incisions.³¹ They saw no difference between the iNPWT- and standard care side at 42, 90, 180 and 365-days follow-up. Furthermore, they established that no differences in trans-epidermal water loss and hydration were seen at the same follow-up moments. Scar colour has thus far not been tested by other

studies and the outcomes in this study showed no difference in erythema and melanin scores at 90 and 365 days. Scar width was not significantly different between the intervention and control side and did not show a more favourable outcome when accounting for any time point. Scar width as an objective measure has been reported twice in clinical studies with mixed results. Nagata et al. showed significantly less wide scars after applying iNPWT for >6 weeks, and Svensson-Björk et al reported no difference between the iNPWT- and standard care side in scar width after 7 days.^{32,33} Therefore, this study suggests that applying negative wound pressure of -80 mmHg for 7 days, according to the working instructions of the specific device, does not affect scar width, pliability and colour.

Seemingly, contradicting outcomes were collected from the POSAS questionnaires. The POSAS Observer scale showed several significantly improved scar parameters for iNPWT after 3 months, whereas the blinded assessments at 12 months showed no significant outcomes anymore. Notably, the mean differences in favour of iNPWT ranged from 0.243 to 1.149 and thus represent only a small beneficial effect. Furthermore, the POSAS Patient scale at 12 months showed improved outcomes for three of the six patient subdomains. Also similar to the observer scale, the mean differences in favour of iNPWT ranged from 0.0068 to 0.1081 and signifies an even smaller effect on the patient scale outcomes. In the literature, the observer and patient scale of the POSAS has also been used before in other clinical studies focusing on the effects of iNPWT on scar quality. Unfortunately, for both the Observer and Patient scale, subgroup outcomes were not always provided. The mean difference in the overall observer score was significantly in favour of iNPWT at 12 months follow-up in the study by Ferrando et al.³⁴ At 42 and 90 days, these significant differences were also seen in the study by Tenaydin et al. for linear scars.³¹ This is in line with the significant outcome seen in this study at 90 days for the *overall impression* and *total score*. In the study by Tenaydin et al., no significant difference was noted at 6- and 12-months follow-up, which was in accordance with this study. The studies by O'Leary et al. and Pellino et al. showed no significant differences in observer scale outcome, respectively, 30 and 90 days after surgery.^{35,36} Importantly, the Observer scale in these clinical studies was non-blinded to the intervention (iNPWT) or did not disclose blinding altogether. In this study, the last observer assessment at 12 months follow-up was blinded and showed no differences in outcomes. In the literature, other clinical studies on iNPWT on scar outcomes present a variety of scar outcome measures such as the Vancouver Scar Scale (VSS),^{33,37} Stony Brook Scar Evaluation Scale (SBSES),^{33,38} Visual Assessment Scale (VAS),^{31-33,35} Manchester Scar Scale (MSS)³⁴ and the BIS (Body Image Scale) with similarly contradicting outcomes.³⁴ Hence, based on the evidence so far with regard to the iNPWT treatment, the observer assessed outcomes of scars remain ambiguous. Therefore, considering the small sizes of the differences seen in this study at 12 months, one can assume that the impact of iNPWT on a scar quality remains small, if present at all.

With regard to the POSAS Patient scale, significant differences in total scores were reported at 42, 90 days by Tanaydin et al. and after 12-months by Ferrando.^{31,34} Other studies reported no significant

differences in patient scale outcomes at 30 and 90 days.^{35,36} Neither did Svensson-Björk et al. observe different outcomes at a mean follow-up of 808 days after surgery.³³ In this study, patients reported the *thickness* of the scar to be better on the iNPWT side during all follow-up moments. At 12 months, *colour*, *pliability* and *thickness* were significantly improved. Colour and pliability were objectively similar in outcomes between the iNPWT and standard care side, and considering the small mean differences seen at this follow-up moment, one should question the clinical significance of these outcomes.

The SCAR-Q outcomes were consistently better for iNPWT, but the level of significance was less consistent throughout the follow-up moments. Significantly better symptoms scales were measured at 30- and 365-days, but not at 90-days follow-up. Reversely, patients only reported significantly better outcomes on the appearance scale at 90-days. Furthermore, the impact of iNPWT was not evidently present in the BODY-Q outcomes and the overall outcomes remained high after surgery, which underlines the notion that gender-affirming mastectomies lead to improved quality of life in transgender men.²⁷ Conclusively, the application of iNPWT showed significant improvements for some patient-reported scar outcomes, bearing in mind that the effect sizes were small.

Another important notion to the outcomes of this study is related to the non-contaminated nature of the type of surgery used in this paper. Although this study showed no clear scar-outcome improvements in gender-affirming mastectomies, it remains possible that these advantages could be present in contaminated types of surgery. As of now, no clear differences have been observed between non-contaminated and contaminated surgery, as no differences were seen in the studies by O'Leary et al., Pellino et al in abdominal laparotomy studies.^{35,36} Future studies will have to be performed to assess the impact iNPWT has on different types of surgery to more specifically state the absence or presence of scar-improving properties of iNPWT.

A limitation of this study was the open-label nature of this study. The impact of attribution bias or placebo effect is difficult, if not impossible, to assess in an open-label study, but might have exaggerated the impact of iNPWT on patient-reported outcomes. This aspect might be attributed to the previously reported positive expectations patients expressed for iNPWT, the increased experienced comfort, and reduced pain which were reported in the primary study.¹⁰ Furthermore, most of the questionnaires used in this study comprised of multiple sub-questions that equated to an overall score. This can result in false significant outcomes based on multiple testing and the non-linear conversion table from absolute value to the 0-100 scale. Furthermore, the power analysis was not based on these specific outcomes, but the sample size was large enough to detect small effect sizes; hence, the sample size seems adequate at distinguishing small, yet significant outcomes. The strengths of this study are that both quantitative and qualitative measures were used to assess effects. The follow-up rates (>92.5%) and response rates (>88.8%) were very high at any moment of measurement. Furthermore, the current trial is, to date, the largest study to have included scar quality outcomes and validated PROMs in a within-patient controlled trial on this subject. The intra-patient randomization allowed for the detection of small effect size, independently from the inter-personal variation.

In conclusion, this within-patient randomised controlled trial has demonstrated that negative pressure wound therapy showed mixed results for quantitative and qualitative scar outcome measures. Incision treated with iNPWT showed several beneficial outcomes in comparison with the standard treatment, albeit with small effect sizes. In quantitative measures, no significant differences were seen when comparing iNPWT to the standard treatment. In the qualitative measures, several outcomes attributed positive effects to iNPWT on scar formation, however, not on postoperative chest satisfaction. It is likely that the actual impact of iNPWT relies heavily on patient experience, and to a far smaller extent, if at all, on quantitative outcomes. Objectively, this suggests that incisional negative pressure wound therapy is of little benefit as a method to improve scar quality.

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CONFLICTS OF INTEREST

E. Middelkoop reports institutional grants from Cutiss AG and MedSkin Solutions Dr. Suwelack for research outside of the submitted work. The other authors do not declare any conflicts of interest that could interfere with the integrity of this study.

AUTHORS'S CONTRIBUTIONS

All authors contributed to the study conception and design and approved the final version to be published and agree to be accountable for all aspects of the work related to its accuracy and integrity. Material preparation, data collection and analysis were performed by F.W. Timmermans and S.E. Mokken. The first draft of the manuscript was written by F.W. Timmermans and all authors commented on previous versions of the manuscript. J.M. Smit and M.B. Bouman also provided their clinical perspective as plastic surgeons. In addition, T.C. van de Grift, M. Mullender and E. Middelkoop acted as study supervisors.

CODE AVAILABILITY

Not applicable, possible in agreement with the corresponding author.

CONSENT TO PARTICIPATE

Informed consent was obtained from all individual participants included in the study.

CONSENT FOR PUBLICATION

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

DATA AVAILABILITY STATEMENT

Not applicable, possible in agreement with the corresponding author.

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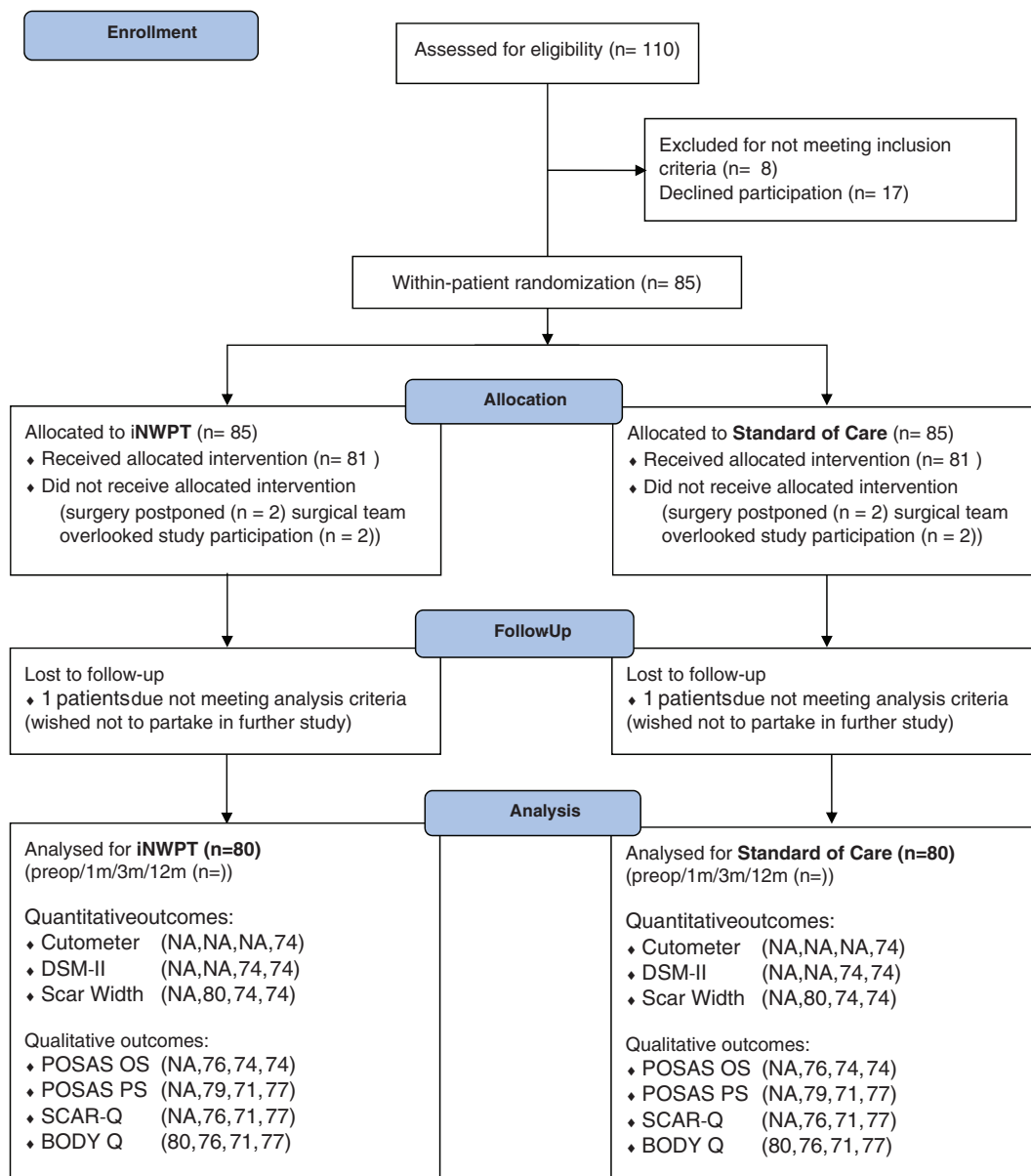
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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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APPENDIX A. CONSORT flow chart for within-patient controlled trials



Abbreviations: DSM-II, DermaSpectrometer; iNPWT, incisional negative pressure wound therapy; OS, POSAS Observer scale; PS, POSAS Patient scale.
 [Color figure can be viewed at wileyonlinelibrary.com]