REVIEW ARTICLE

CONTENTS

Quantitative justification of the advantage of 3d bioprinting over conventional skin transplantation in the reconstruction of burn defects

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ABSTRACT

Aim: To quantify, using published clinical outcome data, the advantage of 3D-bioprinted and bioengineered autologous skin constructs over conventional autologous skin grafting in the reconstruction of burn defects.

Materials and Methods: PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library and ClinicalTrials.gov were searched for records published between 1 January 2015 and 28 February 2026;. Three concept blocks were combined with AND, synonyms within each block with OR: (i) skin graft, autograft, donor site; (ii) burn, thermal injury, full-thickness defect, contracture; (iii) bioprinting, bioengineered skin, skin substitute, dermo-epidermal graft. Randomised trials, cohorts, registries and reviews with pooled data were eligible; excluded were case reports under five patients, in-vitro-only endpoints, no extractable outcome, or non-English records. The tissue economy ratio (TER) is the area of defect closed per unit area of donor tissue harvested, cm^2/cm^2. The iatrogenic donor burden (IDB) is the donor wound area per 100 cm^2 closed, IDB = 100/TER; both are computed only from reported values. Quantitative variables are presented as mean (standard deviation [SD]), median (interquartile range [IQR]), or the min-max range across studies, per how the source reported them; qualitative variables as absolute and relative frequencies.

Results: Forty-six sources were included. Conventional grafting was associated with graft failure in up to 32.3% of patients, post-grafting infection in 41.4%, hypertrophic scarring of the grafted burn area in 8%–67% of patients and of the donor site in 28%-64%, contracture at discharge in 38%-54%, and contracture recurrence in 27.1% of patients at 1 year. In a randomised intra-patient comparison, the tissue economy ratio was 10.76 for a bioengineered autologous dermoepidermal construct versus 1.70 for meshed split-thickness skin grafting, representing a 6.3-fold difference. This corresponded to 9.3 cm^2 versus 58.8 cm^2 of donor wound created per 100 cm^2 of defect closed, respectively, representing an 84.2% relative reduction in donor wound area.

Conclusions: The advantage of the bioprinting-based approach is structural and quantifiable rather than marginal and is greatest in patients with the least donor-tissue reserve. Its adoption is limited less by demonstrated efficacy than by challenges related to vascularisation of large constructs, manufacturing lead times, and regulatory classification.

KEYWORDS: cicatrix, autografts, wound healing, regenerative medicine

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INTRODUCTION

Burn injury causes an estimated 180000 deaths annually against 8.4 million new cases recorded worldwide in a single year, with the burden concentrated in low- and middle-income settings [1, 2]. Skin defects following burns carry the highest prevalence of long-term complications among traumatic wounds [3]. Because acute mortality has fallen steadily, the dominant clinical problem has shifted from survival towards the quality of the skin that is restored and the long-term cost of restoring it.

Hypertrophic scarring or keloids develop in 8-67% of survivors, and pathological scarring approaches 77% in severe injuries requiring repeated operations [4]. Contracture occurs in 38-54% of patients before discharge, and specialised centres report active contractures in 65% of long-term survivors [5, 6]; 5-20% require secondary reconstructive surgery within ten years [7].

International burn-care guidelines state that, after resuscitation, the principal aim is re-epithelialisation, by spontaneous healing or by necrectomy and grafting, to secure the best quality of life after the burn [5]. In practice this is largely minimally invasive: in the Netherlands 45% of hospitalised patients undergo surgery at a median of 15 days, and in Australian/New Zealand centres 47.2% undergo reconstructive surgery within one week [4]. Reconstructive surgery restores range of motion and the protective barrier, and this physical recovery directly affects psychological wellbeing and social reintegration [8].

Despite these benefits, secondary operations carry inherent surgical risks [9]. A fresh graft may fail from poor blood supply, fluid accumulation, or infection, and harvesting healthy skin creates a second wound, causing pain and scarring risk [6]; a good result needs months of compression garments, physiotherapy and splinting [10]. STSG nonetheless remains the reference standard for definitive closure of deep dermal and full-thickness defects [11]; its limitation is structural, since coverage is obtained only by creating this second wound (Table 1). Reconstructed skin rarely reproduces uninjured tissue: colour, texture and thickness may not match, and it typically lacks sweat and sebaceous glands and hair follicles, leaving chronically dry skin needing lifelong care [10].

Three-dimensional (3D) bioprinting and related bio-engineered autologous constructs represent a paradigm shift, uncoupling coverage from large-scale donor-tissue sacrifice: autologous cells are combined with nutrient-rich hydrogels (bioinks) to print new, individually shaped skin layers [11, 13]. Unlike autografting, which leaves a secondary wound the size of the defect, 3D printing needs only a small biopsy and produces a genuine dermis with fibroblasts and extracellular matrix [13]. Trials report significantly less postoperative pain than grafting [11, 14], and since bioink uses the patient's own cells, rejection risk is near zero [11, 13], now supported by randomised evidence rather than laboratory data alone [15]. What has not been done is to place the two families on a common quantitative footing: existing reviews describe each modality separately, none expressing the difference in a single measure of coverage per unit of tissue destroyed.

AIM

To quantify, from published clinical outcome data, the magnitude of the advantage of 3D bioprinted and bio-engineered autologous skin constructs over conventional autologous skin grafting in the reconstruction of burn defects, and to express it through two derived measures: the tissue economy ratio and the iatrogenic donor burden per unit area of defect closed.

MATERIALS AND METHODS

STUDY DESIGN

A structured quantitative comparative synthesis of published clinical outcome data was performed, not a systematic review of treatment effect, since the two families lack a common set of randomised comparisons; the aim was to aggregate reported outcomes within predefined domains and derive comparative metrics.

DATA SOURCES AND SEARCH STRATEGY

PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library and ClinicalTrials.gov were searched for records published between 1 January 2015 and 28 February 2026; earlier publications defining a methodological standard were retained. Three concept blocks were combined with AND, synonyms within each block with OR: (i) skin graft, autograft, donor site; (ii) burn, thermal injury, full-thickness defect, contracture; (iii) bioprinting, bioengineered skin, skin substitute, dermo-epidermal graft. Reference lists were hand-searched.

ELIGIBILITY CRITERIA

Records were included if they reported human clinical outcomes with at least one extractable measure of graft take, wound closure, donor-site morbidity, scar quality, contracture or reoperation, or controlled preclinical bioprinting outcomes with quantified endpoints. Randomised trials, cohorts, registries and reviews with pooled data were eligible; excluded were case reports under five patients, in-vitro-only endpoints, no extractable outcome, or non-English records.

DATA EXTRACTION

Screening proceeded in two stages, titles/abstracts then full texts. Extracted variables were design, sample size, population, intervention, comparator, follow-up and outcome values with dispersion; where a review and its primary study shared a cohort, only the primary source was kept.

DERIVED METRICS

The tissue economy ratio (TER) is the area of defect closed per unit area of donor tissue harvested, cm^2/cm^2. The iatrogenic donor burden (IDB) is the donor wound area per 100 cm^2 closed, IDB = 100/TER; both are computed only from reported values.

STATISTICAL PROCESSING

Quantitative variables are presented as mean (standard deviation [SD]), median (interquartile range [IQR]), or the min-max range across studies, per how the source reported them; qualitative variables as absolute and relative frequencies. No pooled effect was calculated, given heterogeneity of designs and follow-up. Significance levels are reproduced as stated in the sources. Computation used Microsoft Excel and Python 3.11/NumPy 2.4.

ETHICS

This study is based exclusively on publicly available data published in peer-reviewed journals, clinical guidelines

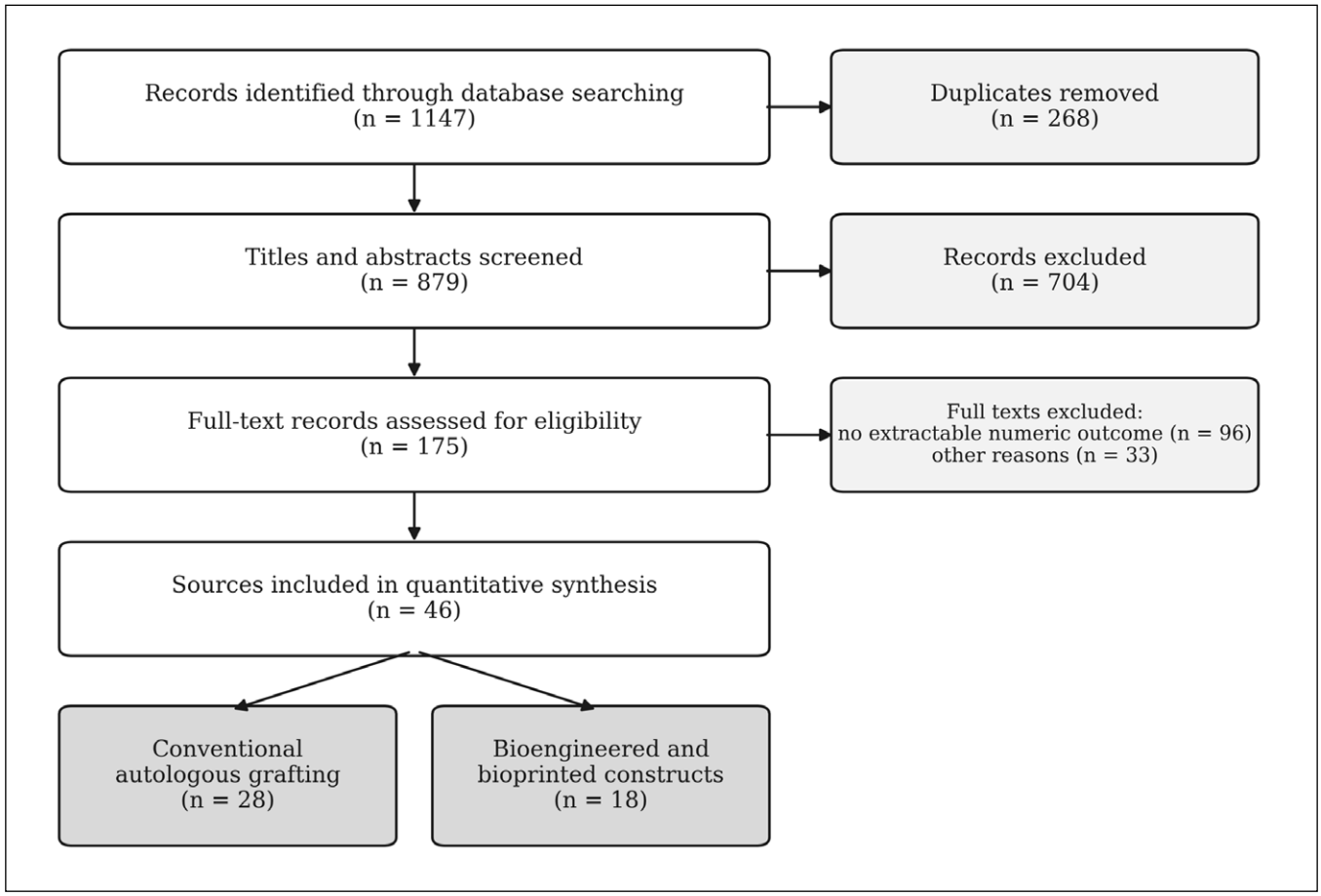


Fig. 1. Flow of source identification, screening and inclusion
Picture taken by the authors

and public trial registries. No patient-identifiable data were used, no clinical intervention was performed and no primary data collection was undertaken; approval by a local ethics committee was therefore not required.

The authors adhered to the Declaration of Helsinki and to international publication-ethics standards, including ICMJE recommendations. No element of this work contains plagiarism, fabrication or falsification of data; all values reproduced here are attributed to their sources.

AI STATEMENT

The following artificial intelligence (AI) tools were used in this work: Elicit and ResearchRabbit, Julius AI. They were used for the following tasks:

- assisted search for literature under the author's control (literature sources were also identified independently by the author);
- assisted generation and adjustment of Python code for data visualisation (figures) under the author's control;

All sections using AI were reviewed and edited personally by the author(s). The scientific statements, conclusions, and results are the author(s)'s own intellectual contribution.

RESULTS

The searches returned 1147 records. After removing 268 duplicates, 879 titles/abstracts were screened and 175 full texts assessed; 46 sources entered the synthesis, 28 on conventional grafting and 18 on bio-engineered or bioprinted constructs (Fig. 1).

THE QUANTIFIED BURDEN OF CONVENTIONAL AUTOLOGOUS GRAFTING

No single failure mode dominated; the burden spread across seven independent domains (Table 1, Fig. 2). Graft failure requiring re-grafting reached 32.3% in a series of 198 patients, where bacterial colonisation was the only independent predictor (odds ratio [OR] 48.34; $p < 0.001$), and infection reached 41.4% [16]. Hypertrophic scarring affected the grafted burn in 8-67% of survivors [4] and the donor site in 28% at eight years and 64% of paediatric patients [12, 17].

Table 1. Quantified outcome burden of conventional autologous skin grafting

Outcome domain	Reported value	Source
Graft failure requiring re-grafting	32.3% of 198 patients	[16]
Post-grafting wound infection	41.4% of cases	[16]
Donor-site hypertrophic scarring	28% at 8 years; 64% of paediatric patients	[12, 17]
Hypertrophic scarring of grafted burn	8-67% of survivors	[4]
Scar contracture at discharge	38-54% of patients	[4, 5]
Contracture recurrence after full-thickness grafting	27.1% at 12 months; 26.9% at 5 years	[18]
Secondary reconstructive surgery within 10 years	5-20% of patients	[7]

Source: compiled by the authors based on [4, 5, 7, 12, 16, 17, 18]

Table 2. Reported outcomes of engineered and bioprinted autologous skin constructs

Parameter	Engineered construct	Meshed STSG control	Source
Expansion ratio, mean (SD)	10.76 (6.03)	1.70 (0.68)	[15]
Clinically relevant scarring, 12 months	none observed	predominantly hypertrophic	[15]
Observer overall scar opinion, 3 months	favours construct; $p = 0.043$	–	[15]
Deviation from normal skin in relief	smaller; $p = 0.005$ at 6 months, $p < 0.001$ at 12 months	–	[15]
Serious adverse events attributable to treatment	2 of 164; both resolved spontaneously	–	[15]
Durability at 5 years, phase I paediatric cohort	maintained; no new safety signals	–	[21]
In situ bioprinting, full-thickness wounds	closure by week 4; 4-5-week acceleration	matrix-only and untreated controls	[24]

Source: compiled by the authors based on [15, 21, 24]

Functional outcomes were equally consistent. Recurrent contracture after full-thickness grafting of joint-involving burns occurred in 27.1% at one year and 26.9% at five years, against 10% and 4.8% after flap reconstruction ($p = 0.043$) [18]. In a paediatric meta-analysis of 532 grafts, full-thickness grafts reduced the odds of post-graft contracture (OR 0.35; $p = 0.0001$) and of surgical release (OR 0.06; $p = 0.00001$) relative to split-thickness grafts, confirming that contracture tracks the quantity of dermis transferred [19]. In a randomised trial grafted surface fell to 92% at twelve months, whereas perforator-based flaps expanded to 142% ($p < 0.001$) [20].

OUTCOMES OF BIO-ENGINEERED AND BIOPRINTED AUTOLOGOUS CONSTRUCTS

Eighteen sources provided quantified outcomes (Table 2). The decisive dataset is a prospective, intra-patient randomised phase IIb trial of an autologous bilayered dermo-epidermal construct against meshed STSG [15]. The mean expansion ratio was 10.76 (SD 6.03) versus 1.70 (SD 0.68) for STSG, a 6.3-fold difference ($p < 0.001$); both areas fully epithelialised by month three, and at twelve months no clinically relevant scarring was observed for the construct, against predominantly hypertrophic STSG controls. Scar opinion favoured the construct at three months ($p = 0.043$), with smaller deviation from normal skin at six and twelve months ($p = 0.005$, $p < 0.001$). Of 164 serious adverse events, only two were attributable to the construct, both resolving spontaneously; five-year paediatric follow-up confirmed durability without new safety signals [21].

Cell-only strategies delimit the effect's boundary. Cultured epidermal autografts supply epidermis without dermis and yield inconsistent take and poor long-term outcomes, requiring three to four weeks of culture [15]. A review of 30 trials in 970 patients confirmed cell therapies accelerate epithelialisation but that dermal reconstitution, not epidermal coverage, is limiting [22], concordant with a dermal-substitute meta-analysis [23]. Preclinically, in situ bioprinting of fibroblasts and keratinocytes into full-thickness wounds produced complete re-epithelialisation by week four, four to five weeks faster than controls [24].

COMPARATIVE TISSUE ECONOMY

Applying the metrics yielded a TER of 1.70 cm^2/cm^2 for meshed STSG and 10.76 cm^2/cm^2 for the engineered construct. As iatrogenic donor burden, closure of a 100 cm^2 defect requires 58.8 cm^2 of donor wound with STSG and 9.3 cm^2 with the construct, an 84.2% relative reduction (Fig. 3). Scaled to a 15% total-body-sur-

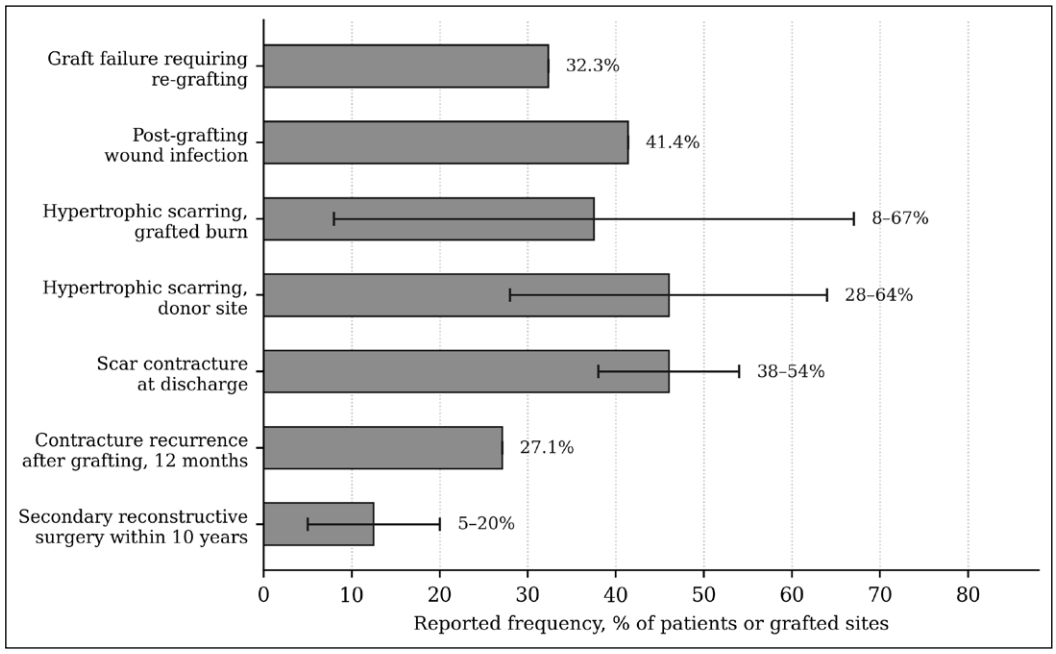


Fig. 2. Reported frequency of adverse outcome domains of conventional autologous skin grafting. Bars show the mid-point of the reported range, whiskers its limits
Picture taken by the authors

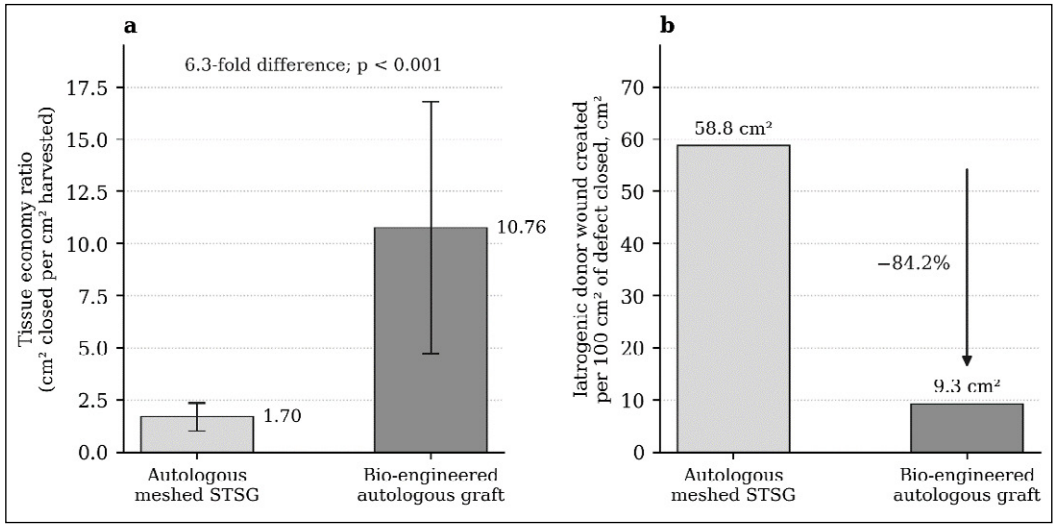


Fig. 3. Comparative tissue economy: (a) tissue economy ratio, mean (SD); (b) iatrogenic donor burden per 100 cm^2 closed.
Picture taken by the authors

face-area burn, about 2700 cm^2 of defect, this is 1588 cm^2 against 251 cm^2 of donor wound, over 7% of total body surface area.

DISCUSSION

The central finding is that the advantage of engineered skin over conventional grafting is structural rather than incremental and can be expressed in a single number. Conventional grafting cannot exceed a tissue economy ratio determined by the degree of mesh expansion applied, and the ratio of 1.70 measured under randomised conditions [15] falls far below the nominal 1:4 ratio because expansion, graft take, and contraction each reduce the effective coverage achieved. Increasing mesh expansion may increase contraction and scar height rather than providing a proportional increase in effective coverage. The engineered construct avoids this limitation because the biopsy serves as a source for cell expansion rather than as a one-to-one source of tissue.

This reframes a long-standing observation: patients rate donor-site morbidity as equal to or worse than the burn scar itself years later [12], consistent with the donor wound representing a structural cost rather than merely a complication. The present analysis quantifies this cost as 58.8 cm^2 per 100 cm^2 of defect closed; reducing it by 84.2% substantially changes the resource requirements of the procedure. Patients with burns involving more than 50%-60% of the total body surface area, in whom donor tissue is particularly scarce, may therefore derive the greatest benefit [11].

Our results extend the existing literature. Reviews of cell-based therapies and dermal substitutes have found that epidermal-only strategies accelerate wound closure without restoring dermal architecture [22, 23]. Our data

provide a quantitative explanation for this limitation: contracture risk is related to the amount of dermis transferred, as demonstrated by the difference in the odds of surgical release between full- and split-thickness grafts [19] and by the divergence in surface area between grafts and flaps at 12 months [20]. This is consistent with evidence that flap reconstruction of paediatric contractures can achieve durable release in cases in which graft reconstruction is associated with recurrence [8]. Data from centres in resource-limited settings, where graft failure reached 32.3% and infection 41.4% [16], further indicate that the burden is greatest where treatment capacity is most limited [1, 2, 9], while engineered constructs remain least available in these settings.

Several limitations apply. The comparison rests on a single randomised trial, 21 enrolled and 13 analysed per protocol, defects no larger than 98 cm^2 under an orphan designation [15]; the metrics are precise but not generalisable to massive burns, and phase III has not been reported. No fully bioprinted construct has completed a randomised comparison against STSG, the evidence being preclinical or first-in-human [24]. Heterogeneity precluded meta-analysis, so ranges describe the literature's spread, not a pooled effect. Nor does TER capture manufacturing time or the deficits bioprinting has not solved: appendage regeneration and a perfusable vascular network anastomosing with host circulation, the chief obstacle to scaling beyond a few hundred cm^2, alongside skin's immunological function in a scaffold [14, 25-29].

Regulatory classification remains unsettled, falling between device and graft, with viability, sterility and release-testing requirements still under harmonisation [14, 26]. A three- to four-week manufacturing time is incompatible with acute resuscitation, confining these constructs to staged reconstruction [15]. Future work should prioritise randomised comparisons beyond 500 cm^2 and health-economic modelling of avoided wounds against manufacturing cost.

CONCLUSIONS

Conventional autologous skin grafting achieves wound closure at a fixed, quantifiable cost: for every 100 cm^2 of defect closed, 58.8 cm^2 of healthy skin is harvested, and the resulting donor sites are associated with hypertrophic scarring in up to 64%-67% of patients, graft failure in up to 32.3%, and recurrent contracture in approximately one-quarter of patients undergoing reconstruction of joint-involving burns.

Bioengineered autologous dermoepidermal constructs, an immediate precursor to 3D-bioprinted skin, achieve a tissue economy ratio of 10.76 compared with 1.70 for meshed STSG in a randomised intra-patient comparison, reducing iatrogenic donor burden by 84.2% and producing no clinically relevant scarring at 12 months.

This advantage is structural rather than marginal and is greatest in patients for whom conventional grafting performs worst. Adoption is limited less by demonstrated efficacy than by the vascularisation of large constructs, manufacturing time, and regulatory classification –priorities for further research.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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