

## REVIEW ARTICLE

# Skin bioprinting for burn reconstruction: From stem cell integration to smart *in situ* regenerative systems

## Supplementary file

Table S1. Summary of key healing outcomes in mouse models from Table 1 studies on skin bioprinting

Study	% Wound closure (Day 7)	% Wound closure (Day 14)	CD31 <sup>+</sup> vessel density	Re-epithelialization score	n/group	Effect direction (wound closure)	Effect direction (angiogenesis)	Effect direction (re-epithelialization)
Ferroni <i>et al.</i> <sup>1</sup>	~58% (Day 10)	~95% (Day 17)	Enhanced angiogenesis evaluated by laminin-immunoreactivity (no quantification); no CD31 staining	Enhanced epidermal thickness; no scoring	5	↑	↑	↑
Hao <i>et al.</i> <sup>2</sup>	>85% (Day 7)	~100% (Day 14)	Increased CD31 <sup>+</sup> IHC, no quantification	Full epidermis + appendages	3	↑	↑	↑
Xu <i>et al.</i> <sup>3</sup>	~79.67% (Day 7)	~100% (Day 12)	Increased CD31 fluorescence intensity (~78%)	Length of neo-epithelial tongue (G-S: 22.80 ± 2.02 mm) Area of neo-epithelium (G-S: 32.33 ± 2.79 mm <sup>2</sup> ) Neo-epidermal thickness (G-S: 147.94 ± 17.37 μm)	3	↑	↑	↑
Fu <i>et al.</i> <sup>4</sup>	~50% (Day 7)	~85% (Day 14)	Increased CD31 <sup>+</sup> capillaries/field: 80 (Day 7) and 50 (Day 14)	Descriptive H&E histology, no score	6	↑	↑	↑
Zhang <i>et al.</i> <sup>5</sup>	~84.6% (Day 7)	~99.2% (Day 14)	Increased CD31 <sup>+</sup> vessels/field: 60.5 ± 6.14 (Day 14)	Descriptive H&E histology, no score	6	↑	↑	↑
Baltazar <i>et al.</i> <sup>6</sup>	Not reported	Qualitative descriptions of healing and scabbing	Increased host-derived (mouse CD31 <sup>+</sup> ) vessels at day 14 (~14%)	Descriptive H&E histology, no score	3	↑	↑	↑
Apelgren <i>et al.</i> <sup>7</sup>	Not reported	Qualitative descriptions of healing; Experimental group 1 (60 days) and group 2 (75 days)	Descriptively observed vascularized fibrous capsule; no CD31 staining	Descriptive H&E histology, no score	Group 1: n = 10 Group 2: n = 11	↑	↑	↑

Table S1. Summary of key healing outcomes in mouse models from Table 1 studies on skin bioprinting

Study	% Wound closure (Day 7)	% Wound closure (Day 14)	CD31 <sup>+</sup> vessel density	Re-epithelialization score	n/group	Effect direction (wound closure)	Effect direction (angiogenesis)	Effect direction (re-epithelialization)
Jorgensen <i>et al.</i> <sup>8</sup>	~91.0% (Day 7)	~100% (Day 14)	Descriptively observed vascularization and vessel lumens	Descriptive H&E histology, no score	4	↑	↑	↑
Seol <i>et al.</i> <sup>9</sup>	~61% (Day 7)	~72% (Day 14)	Descriptively observed vascular network	Descriptive H&E histology, no score	3	↑	↑	↑
Baltazar <i>et al.</i> <sup>10</sup>	Not reported	Not reported; Histological focus, not closure rate	Qualitative perfused CD31 <sup>+</sup> vessels via <i>Ulex europaeus</i> agglutinin I staining	Qualitatively described epidermal maturation and rete ridge formation; no score	Not reported	→	↑	↑
Yanez <i>et al.</i> <sup>11</sup>	Not reported	Not reported; wound contraction focus, not closure rate	Qualitative observation of microvessels	Thickness epidermal (239 ± 35 μm); epidermal layer regeneration (~90%)	5	→	↑	↑
Michael, <i>et al.</i> <sup>12</sup>	Not reported	Qualitative closure was observed (Day 11)	Blood vessels visualized via collagen IV immunostaining; no CD31 staining	Qualitative observation of epidermis formation and integration	3	→	↑	↑

Note: ↑ indicate improvement; ↓ indicate negative effect; and → indicate neutral or non-reported. All results are based on *in vivo* wound healing models. IHC: Effect directions are relative to control groups. From the 15 studies listed in Table 1, three lacked full-text access, resulting in 12 studies included in the final analysis.

Abbreviations: H&E, Hematoxylin-eosin; IHC, immunohistochemistry.

Table S2. Summary of key healing outcomes in large animal models from Table 2 studies on skin bioprinting

Study	% Wound closure (Day 7)	% Wound closure (Day 14)	CD31 <sup>+</sup> vessel density	Re-epithelialization score	n/group	Effect direction (wound closure)	Effect direction (angiogenesis)	Effect direction (re-epithelialization)
Intini <i>et al.</i> <sup>13</sup>	~50% (Day 7)	~100% (Day 14)	Not reported	Qualitative descriptive promotion of epithelialization	12	↑	→	↑
Tanadchangsang <i>et al.</i> <sup>14</sup>	Not reported	Not reported; wound contraction focus, not closure rate	Increased CD31 <sup>+</sup> vessel density (IHC); no quantification	Qualitative descriptive promotion of epithelialization	9	→	↑	↑
Yang <i>et al.</i> <sup>15</sup>	~78% (Day 7)	~94% (Day 14)	Not reported	Epidermis thickness: 37–41 mm; qualitative descriptive promotion of epidermal regeneration and differentiation	3	↑	→	↑

**Table S2. Summary of key healing outcomes in large animal models from Table 2 studies on skin bioprinting**

Study	% Wound closure (Day 7)	% Wound closure (Day 14)	CD31 <sup>+</sup> vessel density	Re-epithelialization score	n/group	Effect direction (wound closure)	Effect direction (angiogenesis)	Effect direction (re-epithelialization)
Wang <i>et al.</i> <sup>16</sup>	~72.2% (Day 8)	~100% (Day 12)	Increased CD31 <sup>+</sup> vessel/mm <sup>2</sup> : 45 (Day 8) and 58 (Day 12); 9.66% CD31 <sup>+</sup> vessel	Regular epithelial layer starts forming (Day 8); Fully formed epithelium (Day 12)	6	↑	↑	↑
Zhou <i>et al.</i> <sup>17</sup>	Rat: ~85% (Day 7)	Rat: ~100% (Day 14); Pig: ~90% (Day 30)	Qualitatively describe increased CD31 <sup>+</sup> vessel density	Epidermis thickness: Rat: mature epithelium with sebaceous glands and follicles Pig: 77–78 mm	Rat: n = 12; Pig: n = 3	↑	↑	↑
Shi <i>et al.</i> <sup>18</sup>	~90% (Day 7)	~100% (Day 14)	Not reported	Enhanced epidermal regeneration (H&E)	3	↑	→	↑

Note: ↑ indicate improvement; ↓ indicate negative effect; and → indicate neutral or non-reported. All results are based on *in vivo* wound healing models. Effect directions are relative to control groups. From the eight studies listed in Table 2, two lacked full-text access, resulting in six studies being included in the final analysis.

Abbreviations: H&E, hematoxylin-eosin; IHC, immunohistochemistry.

**Table S3. Standardized summary of key healing outcomes in mouse models from Table 3 studies on skin bioprinting**

Study	% Wound closure (Day 7)	% Wound closure (Day 14)	CD31 <sup>+</sup> vessel density	Re-epithelialization score	n/group	Effect direction (wound closure)	Effect direction (angiogenesis)	Effect direction (Re-epithelialization)
Yuan <i>et al.</i> <sup>19</sup>	Not reported	Not reported; the study focuses on sweat gland regeneration, not wound closure	Qualitative CD31 <sup>+</sup> staining for vessel formation	Not reported	9–15	→	↑	→
Yao <i>et al.</i> <sup>20</sup>	Not reported	Not reported; the study focuses on sweat gland regeneration, not wound closure	Not reported	Not reported	3	→	→	→
Huang <i>et al.</i> <sup>21</sup>	Not reported; the study focuses on sweat gland regeneration, not wound closure	Qualitative descriptions of wound healing; no quantification	Not reported	Qualitatively describe skin regeneration and epithelial differentiation	5	↑	→	↑
Abaci <i>et al.</i> <sup>22</sup>	Not reported	Not reported; the study focuses on hair follicle regeneration, not wound closure	GFP-HU-VECs, GS-IB4, RBCs, and lumens confirm vascular integration with the host	Qualitatively describe epithelial coverage, tissue integration, and functional differentiation	10	→	↑	↑

Note: ↑ indicate improvement; ↓ indicate negative effect; and → indicate neutral or non-reported. Effect directions are relative to control groups.

Abbreviations: GFP-HUVECs, green fluorescent protein-labeled human umbilical vein endothelial cells; GS-IB4: *Griffonia simplicifolia* isolectin B4 (commonly used for labeling mouse vascular endothelial cells); RBCs, red blood cells.

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