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Bioengineered Tools for Tissue Expansion: A Systematic Review of Tissue Growth and Surgical Outcomes

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ABSTRACT

Tissue expansion is used during reconstructive surgery when additional healthy tissue is needed for repair. Bioengineered devices, computational models, biomaterials, and cell-based methods may support tissue expansion or regenerative repair. This review examined research identified through searches reported between January 9 and April 1, 2026. Of 271 PubMed results, 205 records were screened; 66 were not screened because of time limitations. Forty reports were sought, 32 full texts were assessed, and 21 studies met the eligibility criteria after reassessment during revision. Animal experiments showed intestinal lengthening with spring-based devices, while modeling studies evaluated skin strain and estimated growth. One ex-vivo study demonstrated immediate mechanically induced tissue stretching, but not biological growth. Scaffold and cell-based approaches produced several promising results in animal or laboratory models, including bone regeneration and in-vitro wound-gap closure. However, device stability, differences between experimental models, and limited human clinical evidence restrict the conclusions. Because screening was incomplete and most outcomes were preclinical, the findings are preliminary and do not establish superiority over standard reconstructive treatments.

INTRODUCTION

Tissue expansion is used during reconstructive surgery when there is not enough healthy tissue to repair a damaged area. Traditional tissue expansion often involves placing a device that gradually stretches the surrounding tissue. Over time, the tension may stimulate growth, but the amount of force, the length of treatment, and how the tissue responds can all affect the result [1,6,8,10]. Bioengineering may help researchers understand and control these factors, although improvements in patient outcomes still need to be tested.

Researchers have studied different ways to expand tissue or support repair. Spring-based devices apply force to lengthen intestinal tissue in animal models [2–5,7,9,11–13,15,16]. A separate sleeve-based experiment measured immediate mechanical extension of tissue taken from deceased rats [21]. Computational modeling and strain measurements estimate how skin responds to force and where greater stress may occur [1,6,8,10]. Other experiments use scaffolds, hydrogels, microspheres, or cell-based methods to support regenerative repair and test cellular behavior in wound-healing models [12,14,17–20].

These approaches measure different outcomes and should not be considered interchangeable evidence of clinical effectiveness.

Because research on these methods has been conducted in different tissues and experimental models, it can be difficult to compare the findings. Many studies use animals, laboratory cultures, or computer simulations rather than human clinical trials. This review brings these studies together to examine the evidence for mechanical tissue expansion and related regenerative methods, while considering their limitations and possible relevance to future reconstructive surgery.

METHODS

Search strategy

PubMed was the only database searched for peer-reviewed research related to bioengineering and tissue expansion. The searches were carried out between January 9 and April 1, 2026. Terms used during the project included "tissue expansion," "bioengineering," "mechanical tissue expansion," "intestinal lengthening," "skin expansion," "scaffold," "hydrogel," "biomaterial," "stem cell," and "regenerative medicine." The search yielded 271 PubMed records. The exact Boolean search strings and detailed search history were not retained, which limits reproducibility. No additional databases were searched.

Eligibility criteria

Eligible publications were original peer-reviewed research articles written in English and published in 2000 or later. Human, animal, laboratory, and computer-based studies were considered when they focused directly on tissue expansion, tissue growth, or regenerative reconstruction; examined a bioengineered tool, material, device, or method; and reported measurable or meaningful outcomes related to growth, healing, repair, reconstruction, or possible surgical use. Reviews, editorials, other non-peer-reviewed reports, articles before 2000, and non-English publications were excluded. Studies limited to cell isolation or laboratory expansion without a clear tissue-growth or repair application, unrelated diseases, purely material measurements without a directly relevant growth or repair endpoint, or insufficient relevant results were also excluded. Eligibility was reassessed during revision using these criteria to resolve inconsistencies between included and excluded studies.

Table 1. Inclusion and exclusion criteria used for study selection

Inclusion criteria	Exclusion criteria
Peer-reviewed original research article	Non-peer-reviewed sources
Articles written in English	Articles not written in English
Published in 2000 or later	Published before 2000
Human, animal, laboratory, or computer-based studies	Review papers, editorials, narrative reviews
Direct focus on tissue expansion, tissue growth, or regenerative reconstruction	Cell isolation or cell expansion only, without a clear tissue repair or tissue growth use

Inclusion criteria	Exclusion criteria
Examination of a bioengineered tool, material, device, or method	Studies focused on unrelated diseases or topics outside the scope of this review
Outcomes connected to tissue growth, healing, reconstruction, or possible surgical use	No direct outcome related to tissue expansion, tissue growth, regenerative repair
Studies that provided measurable or meaningful results related to tissue expansion or repair	Insufficient information to answer the research question or not enough data available.

Screening and selection

The PubMed search returned 271 results. One reviewer screened 205 titles and abstracts; the remaining 66 records were not evaluated due to time constraints, and their eligibility is unknown. Of the 205 screened records, 165 were excluded and full texts were sought for 40 reports. Eight could not be retrieved. Thirty-two full-text reports were assessed. After reassessing the eligibility criteria during manuscript revision, 11 reports were excluded and 21 studies remained in the qualitative synthesis. This revised set added Kargozar et al. (2017), which measured bone regeneration in rats, and Meyer et al. (2023), which measured immediate mechanical tissue extension ex vivo. Three originally included reports were removed because they did not meet the direct tissue-growth or repair outcome interpretation applied during revision. These changes revised the original selection of 22 studies to 21. Figure 1 summarizes the study-selection process.

Data extraction and synthesis

For each included study, the tissue type, experimental model, bioengineered approach, main findings, and key limitations were recorded. Studies were compared qualitatively because their methods, populations, and outcomes differed substantially. Results were organized into overlapping categories of mechanical tissue expansion, bioengineered materials and scaffolds, and cell-related regenerative approaches. No pooled treatment effect was calculated, and evidence from animal models, cell cultures, and simulations was kept separate from human clinical effectiveness. A formal, standardized risk-of-bias assessment was not documented for these studies.

RESULTS

Study selection and characteristics

Of 271 identified PubMed results, 205 records underwent initial screening, 40 full texts were sought, and 32 were assessed. Eleven full-text reports were excluded after the eligibility reassessment, leaving 21 included studies. Sixteen examined mechanical tissue expansion, mechanical stretching, or related modeling; six involved materials, scaffolds, or hydrogels; and five assessed cell-related regenerative approaches. These groups overlap and should not be added together. Evidence was dominated by animal experiments, ex-vivo tissue tests, laboratory studies, and computational analyses, with no adequate direct comparison establishing improved reconstructive outcomes in human patients. Table 2 summarizes the included studies and their limitations.

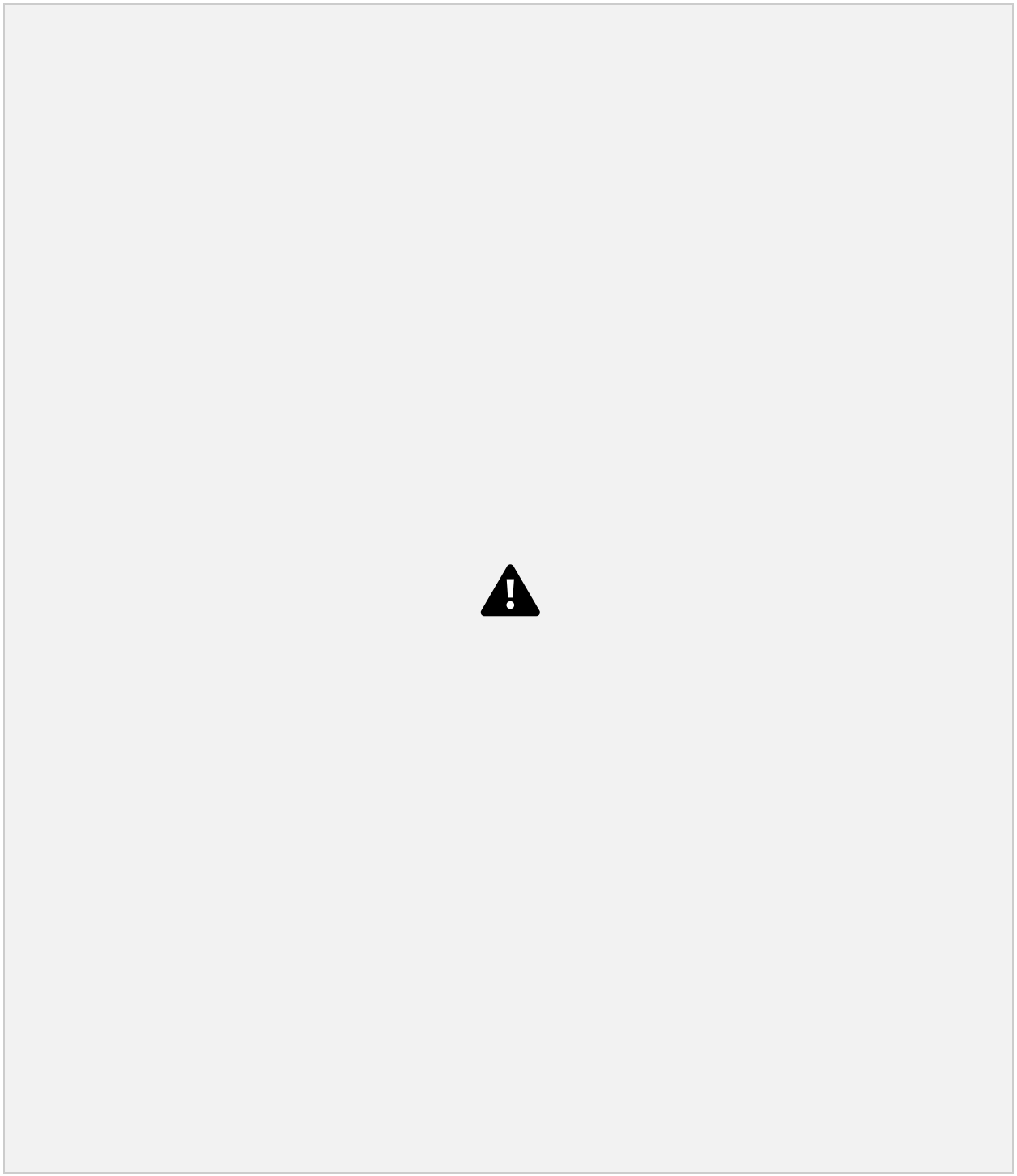


Figure 1. Study selection after reapplying the stated eligibility criteria during revision. The 66 unreviewed records were not excluded on the basis of eligibility.

Mechanical tissue expansion

The clearest direct evidence of tissue lengthening came from spring-based intestinal experiments. In juvenile pigs, Huynh et al. [2] reported approximately 1.47-fold intestinal lengthening, but five springs detached prematurely. Another porcine study reported substantial bowel lengthening while also observing frequent device slippage [7]. Rat models showed the potential for repeated expansion [16] and simultaneous lengthening of two intestinal segments [13]. These results show that mechanical force can produce tissue lengthening in animals, but device displacement and questions about intestinal function remain concerns. Meyer et al. [21] also tested a sleeve-based mechanical expander in tissue from seven deceased rats and reported a 32.5 ± 23.6% immediate increase in canal length. However, the tissue wall became thinner and the mucosal lining was disrupted. Because the experiment was ex vivo, these measurements demonstrate immediate stretching rather than biological tissue growth, permanent lengthening, or safety in living animals. Skin expansion studies used imaging and modeling to examine expansion schedules, reversible stretching, estimated growth, and regional strain [1,6,8,10]. Those results help explain tissue behavior but do not demonstrate fewer surgical complications in patients.

Biomaterials, scaffolds, and hydrogels

Bioengineered materials were investigated as supports for cells or for the repair of injured tissue. In a rat intestinal model, bFGF-releasing microspheres increased some vascular and enteric-ganglion measurements without a statistically significant additional increase in bowel length [12]. Porous microspheres supported short-term mesenchymal stem-cell retention in an injured rat heart, although functional heart recovery was not measured as a successful regenerative outcome [14]. In a rat cranial-defect model, Kretlow et al. [19] found that cells delivered with some scaffold combinations improved bone-volume measurements. Kargozar et al. [20] observed more new bone formation with modified stem cells and bioactive glass/gelatin scaffolds than with the comparison scaffolds; the authors reported approximately 90.0 ± 2.4% new bone formation relative to defect area in the strongest treatment group. These were animal findings, not evidence of improved reconstruction in human patients.

Cell-based and in-vitro wound-healing outcomes

Some studies used laboratory assays to examine biological processes relevant to wound repair. Esteban-Vives et al. [17] found that human fetal-derived dermal cells showed rapid in-vitro wound-gap closure in a scratch assay, but the study also raised concerns about maintaining cell-lineage stability during expansion. Mogha et al. [18] reported that skin-like elastic hydrogels supported keratinocyte proliferation and tested cell function with a laboratory wound-healing assay. Together with the cell-delivery and bone-regeneration experiments [14,19,20], these results suggest possible roles for bioengineered approaches in regenerative research. However, a scratch assay measures cultured cell migration and coverage, not healing of a patient's wound, and no clinical advantage can be concluded from these results.

DISCUSSION

The studies suggest that controlled mechanical force can lengthen tissue in experimental settings and that some engineered materials can affect biological processes involved in tissue growth and repair. These forms of evidence should not be treated as equal. Measured intestinal lengthening in a living animal does

not establish normal long-term digestive function, and an in-vitro wound-gap assay does not demonstrate faster healing in a patient. Similarly, the immediate stretching seen in Meyer et al. [21] was measured in tissue from deceased rats, so no biological adaptation or long-term safety was demonstrated; tissue thinning and changes to the mucosal lining also raise questions about injury. Device slippage, premature spring detachment, and changes in enteric nerve measurements deserve attention before these strategies can be translated into clinical practice [2,7,11]. While modeling and laboratory methods can guide future devices or cell therapies, clinical effectiveness and long-term safety have not been established by the included studies.

This review has important limitations. PubMed was the only database searched, so studies indexed elsewhere may have been missed. Only 205 of 271 PubMed results were screened; the other 66 were left unreviewed because of time constraints, so relevant studies may have been missed. Eight sought reports could not be retrieved. Screening and eligibility decisions were conducted by one reviewer, and there was no independently documented duplicate screening or formal standardized risk-of-bias assessment. The eligibility decisions were revisited during revision, including correcting inconsistent treatment of material-only, cell-expansion-only, and mechanical-stretching studies. Research models, tissue types, outcomes, and observation periods varied substantially, so studies were not pooled and meaningful comparisons with traditional clinical methods were not possible. Some studies, including the ex-vivo expansion experiment, could not measure healing or tissue growth over time. Most of the evidence came from animals, laboratory models, or computer simulations. The results should therefore be treated as an exploratory, incomplete systematic review rather than an exhaustive evaluation of all available evidence.

CONCLUSION

Bioengineered methods may support tissue expansion and regenerative repair through mechanical force, scaffolds, and cell-related approaches. Animal studies provide evidence of tissue lengthening and selected regeneration outcomes, while modeling, ex-vivo, and in-vitro experiments help explain the behavior of tissues, materials, and cells. Immediate stretching in nonliving tissue should not be confused with biological tissue growth. Unanswered questions remain about device stability, tissue injury, long-term function, and safety in patients. Because screening was incomplete and clinical evidence was limited, the findings are preliminary rather than proof that these techniques are better than standard reconstruction. Further clinical research with longer follow-up and more complete evidence screening is needed.

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APPENDIX

Table 2. Characteristics, findings, and limitations of included studies

Abbreviations: PCL, polycaprolactone; MSC, mesenchymal stem cell; bFGF, basic fibroblast growth factor. Category assignments overlap; no formal risk-of-bias grades are implied.

Study	Tissue / model	Bioengineered approach	Main finding	Major limitation
[1] Lee et al. (2018)	Porcine skin; expansion protocols and computational analysis	Four porcine skin-expansion protocols assessed with 3D photography and computational growth modeling.	Quantified how changes in expansion volume and duration affect skin deformation and estimated growth.	Porcine/model-derived findings; no prospective human surgical outcomes.
[2] Huynh et al. (2016)	Jejunum; juvenile Yucatan pigs	Biodegradable PCL springs placed in bowel continuity.	Measured 1.47-fold intestinal lengthening and increased crypt depth and muscularis thickness.	Five springs detached prematurely; animal feasibility study.
[3] Portelli et al. (2022)	Cecum/large intestine; mice	Compressed nitinol springs used for colonic distraction enterogenesis.	Spring-treated cecal segments reached about 150% of initial length, supporting colonic feasibility.	Small-animal model with outcomes measured at 7–14 days; no clinical functional data.
[4] Rafeeqi et al. (2022)	Ileum; juvenile Yucatan pigs	Spring-mediated mechanical distraction in the ileum.	Demonstrated ileal lengthening in a large-animal model and examined tissue preservation.	Preclinical study; effectiveness and functional benefit in patients not established.
[5] Rafeeqi et al. (2023)	Jejunum; Yucatan minipigs	Eclipse XL1 intraluminal nitinol spring with follow-up to 180 days.	Lengthening persisted after spontaneous device passage; no device-attributed obstruction or overt perforation reported.	Small preclinical sample; did not establish safety or effectiveness in human patients.
[6] Buganza-Tepole et al. (2014)	Expanded skin flaps; finite-element simulation	Modeled direct-advancement and double-back-cut flaps in different orientations.	Predicted stress distributions varied by flap design and tension-line orientation.	Idealized simulation; reductions in human surgical complications were not tested.

Study	Tissue / model	Bioengineered approach	Main finding	Major limitation
[7] Rafeeqi et al. (2022)	Jejunum; pigs	Internal plication sutures to confine expanding intestinal springs.	Spring-treated bowel lengthened by an average of 72% from baseline.	Five of seven springs slipped from fixation sites, reducing consistency.
[8] Purnell et al. (2018)	Skin; two minipigs	Skin expansion combined with isogeometric growth/stretch analysis.	Slower expansion yielded more estimated tissue growth; rapid expansion produced more reversible stretch.	Only two animals; model-derived growth estimates and no human validation.
[9] Sullins et al. (2014)	Isolated jejunal segments; rats	Biodegradable PCL spring for mechanical intestinal lengthening.	Mean segment length rose from 1.0 cm to 2.7 cm; restored segments displayed peristalsis.	Preclinical isolated-segment model; fewer enteric ganglia were observed.
[10] Buganza Tepole et al. (2017)	Skin; porcine imaging model	Multiview stereo imaging and isogeometric analysis of regional strain.	Demonstrated a technique for mapping local strain during skin expansion.	Primarily a measurement protocol; no proof that using it improves clinical outcomes.
[11] Sullins et al. (2014)	Jejunum; rats	Degradable PCL springs in a Roux-en-Y intestinal model.	Jejunal segments lengthened from roughly 1.0 to 3.0 cm; muscle thickness and crypt depth increased.	Fewer submucosal ganglia; subsequent functional outcomes not established.
[12] Rouch et al. (2016)	Jejunum; rats	PCL springs with bFGF-releasing microspheres.	Increased vascular density, crypt depth and enteric ganglion measures relative to blank microspheres.	No statistically significant added lengthening; only 10 rats studied.
[13] Scott et al. (2016)	Jejunum; rats	Two PCL springs used in series in a Roux limb.	Two segments lengthened simultaneously, reaching a combined mean length of 45 mm.	Segments lengthened unequally; anchoring loops produced inflammation.

Study	Tissue / model	Bioengineered approach	Main finding	Major limitation
[14] Lee et al. (2015)	MSCs; laboratory cultures and rat heart-injury model	Porous PLGA/PEI microspheres for human mesenchymal stem-cell delivery.	Improved cell attachment in culture and donor-cell engraftment at two weeks in rat hearts.	Short follow-up and primarily engraftment outcomes; functional tissue repair not established.
[15] Portelli et al. (2021)	Jejunum; mice	Compressed nitinol springs in a defunctionalized Roux limb.	Spring-treated bowel reached about 240% of baseline length versus 120% in controls; tissue growth markers increased.	Mouse model with 14–21-day assessment; long-term function unknown.
[16] Scott et al. (2015)	Jejunum; rats	Sequential PCL spring placement to re-lengthen previously expanded tissue.	Previously lengthened intestine lengthened again; higher spring force was needed in the second round.	Rodent model; multiple-procedure safety and function in patients unknown.
[17] Esteban-Vives et al. (2019)	Human fetal-derived dermal cells; laboratory cultures	Isolation, expansion and characterization for possible wound-healing cell banking.	Fetal-derived dermal cells showed rapid gap coverage in an in-vitro scratch assay and related wound-healing features.	Laboratory wound-gap closure is not patient healing; cell-lineage stability during expansion was a concern.
[18] Mogha et al. (2019)	Human keratinocytes; laboratory culture	Soft hydrogel substrates engineered to mimic natural skin elasticity.	Skin-like hydrogels supported keratinocyte proliferation and cell function in an in-vitro wound-healing assay.	Cell-culture evidence only; no demonstrated improved skin healing in human patients.
[19] Kretlow et al. (2010)	Rat cranial bone defects; 12-week experiment	Uncultured bone-marrow mononuclear cells in fibrin hydrogels and porous scaffolds.	Cells improved bone-volume outcomes; some cell-loaded PLLA scaffolds improved mechanical attachment; PRP added no benefit.	Effects depended on scaffold/outcome; animal study cannot establish human benefit.

Study	Tissue / model	Bioengineered approach	Main finding	Major limitation
[20] Kargozar et al. (2017)	Cranial bone defects; 15 rats	Bioactive glass/gelatin scaffold seeded with mesenchymal stem cells expressing BMP-7	The modified stem-cell/scaffold group had greater bone formation; authors reported 90.0 ± 2.4% new bone formation by histomorphometry.	Small animal study, 12-week follow-up; no evidence for better patient outcomes.
[21] Meyer et al. (2023)	Vaginal-canal tissue from seven deceased rats; ex-vivo feasibility test	Spring-like vaginal expansion sleeve (VES), with immediate length measurements and histology.	Mean immediate extension of 5.36 ± 1.18 mm (32.5 ± 23.6%); measured mechanical stretching, not tissue growth.	Nonliving tissue; immediate-only findings, tissue-wall thinning and mucosal disruption; no healing, sustained growth, or patient outcomes.