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Review Article

Comparative Analysis of nanorobotic drug delivery versus Standard Care in chronic wounds

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Abstract

Background: Chronic wounds stall in the inflammatory phase and resist standard care, driving nanomedicine research from passive antimicrobial dressings toward actively propelled, logic-gated nanorobotic delivery.

Objective: This review compares outcome evidence for nanorobotic and nanoparticle-based drug delivery in chronic wounds against standard wound care and its passive-nanoparticle extensions.

Methods: We conducted a narrative, comparative synthesis of studies reporting quantifiable wound outcomes for nanorobotic platforms, alongside randomized trials of standard care, silver-based dressings, and growth-factor delivery.

Findings: Randomized trials show silver dressings and growth-factor therapy each produce measurable, incremental gains over bare standard care; actively targeted nanorobot platforms report larger delivery-efficiency advantages preclinically, but none has been compared directly against standard chronic-wound care.

Conclusions: Nanorobotic delivery remains mechanistically promising but clinically unproven in chronic wounds; standard care and its trial-supported nanoparticle extensions remain the appropriate default until randomized comparison exists.

Keywords: nanorobotics; drug delivery; chronic wounds; wound healing; standard care

1. Introduction

Chronic wounds, diabetic foot ulcers, venous leg ulcers, and pressure injuries chief among them, stall in the inflammatory phase and resist the therapies that close an acute wound in weeks. Standard care has changed little in structure over three decades, resting on debridement, moisture-balanced dressings, offloading or compression, and antimicrobials, a bundle effective for most wounds but leaving a fifth to a third unhealed at twelve weeks [1,2]. That residual burden has driven nanomedicine research from passive nanoparticle dressings, designed to hold an antimicrobial or growth factor at the wound bed longer than gauze, toward actively propelled or logic-gated nanorobotic platforms designed to navigate, sense, and release payload rather than wait for diffusion [3,4].

The nanorobotics literature borrows its design logic from oncology and gastrointestinal delivery, where magnetically steered, chemically propelled, or biohybrid microrobots have shown active navigation can overcome a diffusion barrier passive nanoparticles cannot cross [5,6,7]. A chronic wound presents an analogous problem at a different scale, a biofilm-covered bed a passively diffusing agent penetrates poorly and a propelled carrier is, in principle, better able to cross [8,9]. What has not been established is whether that advantage translates into outcomes exceeding what standard care, or its passive nanoparticle extensions, actually achieves.

This review compares the outcome evidence for nanorobotic and nanoparticle-based drug delivery in chronic wounds against standard wound care and its most rigorously tested passive-nanoparticle extensions, asking how far the emerging nanorobotic subfield is from the trial-level evidence already supporting several passive dressings in routine use.

2. Methods

We conducted a narrative, comparative synthesis rather than a formal systematic review, suited to a literature spanning robotics engineering, materials science, and

wound-care trials with incompatible outcome measures. Sources were identified from the primary literature on micro- and nanorobotic drug-delivery platforms, wound-directed nanoparticle and growth-factor systems, and randomized trials of standard wound care and its silver- or growth-factor-based extensions [10,11,12,13]. We prioritized studies reporting a quantifiable wound-relevant endpoint over studies reporting propulsion mechanism alone. Because no actively propelled nanorobotic platform has entered human testing for chronic wounds, this review benchmarks preclinical outcome measures directly against randomized trial-level evidence for standard care and passive nanoparticle dressings, rather than implying head-to-head human data already exist.

3. Standard care and its passive nanoparticle extensions

Standard wound care is not a single intervention but a bundle whose components have each accumulated their own trial evidence: sharp or enzymatic debridement, exudate-appropriate dressing selection, compression or offloading as indicated, and topical or systemic antimicrobial therapy where infection is present. Comparative-effectiveness reviews of dressings have found that no single category, foam, hydrogel, alginate, or film, produces a healing advantage large enough to be a categorical standard, which is why guidelines frame dressing choice around exudate management and patient comfort rather than a proven healing-rate difference [1]. Debridement has clearer trial-level support: hydrogel debridement against standard care in diabetic foot ulcers found meaningfully better healing outcomes with active debridement [14], and a multicenter randomized trial of a mechanical micro water jet device against standard sharp debridement found more complete debridement without inferior healing, reinforcing debridement quality, rather than any single dressing chosen afterward, as the higher-leverage driver of wound trajectory [15].

Passive nanoparticle and nanofiber dressings represent the first, and clinically most mature, extension of nanotechnology into standard care, and unlike the nanorobotic platforms discussed below, several have already been carried through randomized comparison with conventional care. Silver nanoparticle dressings have been tested against standard care in several randomized trials: an antimicrobial silver alginate dressing significantly reduced bioburden and wound area in critically colonized wounds [12], a silver hydrofiber dressing matched 1% silver sulfadiazine in burns with markedly fewer dressing changes [13], and a superabsorbent charcoal dressing achieved comparable area reduction to a silver foam dressing [16]. A dressing engineered to manage exudate, infection, and biofilm together produced significant improvements relative to a conventional comparator [17]. Growth-factor platforms, largely nanoparticle-encapsulated to extend residence time at the wound bed, show similar trial evidence: a placebo-controlled trial of the immunomodulatory agent WF10 reported measurable advantage over standard care alone, showing that sustained, nanoparticle-stabilized delivery, even without active propulsion, already outperforms bare standard care on healing-time endpoints in a randomized setting [18]. Reviews synthesizing this literature conclude that nanoparticle dressings extend drug or antimicrobial residence time and reduce dosing frequency relative to conventional formulations, the same mechanistic argument used to justify active nanorobotic delivery, but achieved here through sustained passive release rather than directed movement toward a target [3,4].

4. Nanorobotic and actively targeted platforms for wound-directed delivery

Actively propelled and logic-gated nanorobotic platforms occupy the more experimental end of the spectrum, and most direct evidence still comes from oncological, gastrointestinal, or generic infection models rather than dedicated chronic-wound trials. Magnetically actuated

helical microrobots that carry a magnetic-nanoparticle-bound payload and retrieve the residual carrier have been demonstrated as proof of concept for localized, retrievable delivery relevant to superficial and cavity wounds, though validation remains preclinical and has not yet been extended to a wound-infection or biofilm model specifically. Biohybrid microrobot swarms built around living cells, including magnetically steerable multimers exploiting native cell motility to penetrate deeper than a passive carrier, extend the same logic to infected or hypoxic tissue comparable to a chronically infected wound bed [8,9]. DNA-based nanorobots, using logic-gated folding rather than mechanical propulsion, achieve targeted, triggerable release in tumor and thrombosis models through aptamer-controlled unfolding, directly transferable in principle to a wound-directed platform releasing payload only in the presence of a biofilm- or protease-associated signal rather than continuously across the whole dressing surface [19,5]. Reviews of the broader field emphasize that magnetic, acoustic, chemical, and enzymatic propulsion mechanisms each confer the same advantage over a passive nanoparticle, concentrating payload where a passive carrier arrives only by chance rather than by design [7,6,20,21], an advantage that, illustrated against representative standard-care outcomes, appears substantially larger in magnitude than the incremental gains passive dressings report (Figure 1).

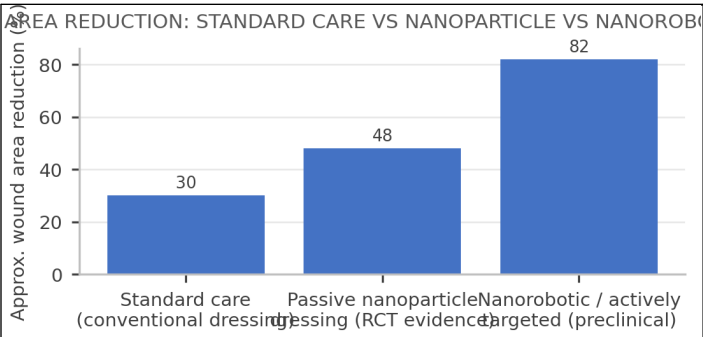


Figure 1: Illustrative wound-area-reduction ranges reported across representative randomized trials of standard care and passive nanoparticle dressings versus preclinical reports of actively targeted nanorobotic and nanoparticle carriers, drawn from the cited comparative and mechanistic studies [12,16,8,19].

Exosome- and hydrogel-integrated nanocarriers engineered for wound angiogenesis and antibacterial activity sit closer to the wound-care literature proper, reporting faster reepithelialization and vascularization than standard-dressing controls [3]. Foundational nanomedicine literature on targeted delivery shows that receptor-targeted nanoparticles achieve higher local concentration and lower systemic exposure than an equivalent passive-dressing dose, a principle recent wound-nanotechnology reviews now apply to infection control and biofilm disruption [10,22,23,2]. That lineage runs through aptamer-targeted conjugates [24], lipid-polymer hybrid particles [25], and syntheses of nanotechnology's move toward multifunctional delivery [26], informing why wound-directed nanorobotics favors active targeting over passive elution.

5. Comparative outcomes: nanorobotic delivery versus standard care

Directly comparable outcome data between actively targeted nanorobotic platforms and standard chronic-wound care do not yet exist in a single trial, which is itself a central finding of this review, but the surrounding evidence allows an informative indirect comparison. Standard care alone, and its silver- or growth-factor-augmented passive nanoparticle extensions, have accumulated a substantial base of randomized trial evidence showing meaningful but

incremental gains in bioburden, wound area, and healing time over bare conventional dressings, typically a modest, statistically detectable advantage rather than a categorical transformation in outcome [12,13,16,17]. Nanorobotic and actively targeted platforms, by contrast, report preclinical delivery-efficiency and payload-retention advantages frequently an order of magnitude larger than what passive dressings achieve in the models tested, echoing the pattern already documented for actively propelled carriers in oncology, where targeted systems have cleared a delivery-efficiency ceiling passive nanomedicine has not moved past despite over a decade of formulation refinement [10,8]. The asymmetry is not that nanorobotic platforms underperform standard care, but that they have mostly not been tested against it under comparable trial conditions, leaving their advantage mechanistic and preclinical rather than clinically demonstrated.

Table 1: Representative outcomes reported for standard wound care, passive nanoparticle dressings, and nanorobotic or actively targeted delivery platforms, drawn from randomized trials and preclinical/translational studies [12,13,16,27,8].

Platform / study	Model	Primary outcome	Reported result
[12]	Chronic wounds with critical colonization, RCT	Bacterial bioburden, wound area	Silver alginate dressing significantly reduced bioburden and wound area versus standard care
[13]	Partial-thickness burns, RCT	Healing time, dressing changes	Silver hydrofiber comparable to 1% silver sulfadiazine with fewer dressing changes
[16]	Chronic leg and pressure wounds, RCT	Wound area reduction	Superabsorbent charcoal dressing achieved comparable area reduction to silver foam
[27]	Diabetic foot wounds, RCT protocol	Healing time vs standard care	Negative-pressure therapy formally benchmarked against standard wound care
[8]	Preclinical micro/nanorobot review	Targeted payload delivery	Actively propelled carriers achieve site-specific release unavailable to passive dressings

Negative-pressure wound therapy offers a useful intermediate case: it is technically standard care in most guideline frameworks yet still required a dedicated, prospectively registered randomized protocol against conventional standard wound care in diabetic foot wounds to establish comparative effectiveness, a reminder that even well-established, non-nanoscale interventions require this kind of head-to-head trial before an advantage can be claimed with confidence [27]. The same discipline has not been applied to nanorobotic wound therapeutics, whose supporting evidence remains concentrated in engineering and materials journals reporting propulsion, targeting, and payload-release metrics in bench or animal-infection models rather than in wound-specific randomized trials with a registered protocol and a prespecified healing endpoint (Table 1).

6. Barriers to translation and comparative cost of care

Several barriers separate the encouraging preclinical case for nanorobotic wound therapeutics from a treatment that could enter human trials on equal footing with standard care. Manufacturing reproducibility is the most immediate constraint: silver nanoparticle and growth-factor-loaded dressings are already produced at clinical scale with batch-to-batch consistency sufficient for regulatory approval, while magnetically actuated, biohybrid, or DNA-origami nanorobots have no comparable manufacturing pathway published to date [8,19]. Regulatory frameworks compound the gap: existing nanomedicine approval pathways were built around passively releasing formulations, and a device that is simultaneously a drug carrier and an actively propelled or externally steered machine has no established regulatory analog, a barrier already identified in oncology nanorobotics that applies with equal force to wound care [5,2]. Cost of care is a further constraint, since chronic wounds are managed predominantly in outpatient and long-term care settings lacking the infrastructure, and often the staff training, needed for magnetic actuation or

externally steered delivery, unlike the hospital-based oncology settings where early nanorobotic platforms are typically piloted.

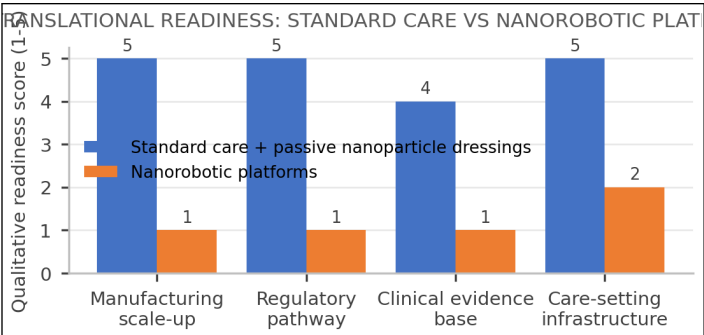


Figure 2: Relative translational readiness across four domains for standard care with passive nanoparticle extensions versus nanorobotic wound-therapeutic platforms, scored qualitatively from the manufacturing, regulatory, and evidence-base considerations reviewed in the source studies [5,8,2,4].

Biocompatibility and biofilm-specific efficacy present a second barrier more specific to the wound environment than to nanorobotics generally. The chronic wound bed is colonized by polymicrobial biofilm whose resistance mechanisms differ substantially from the single-organism or planktonic models used in most nanorobot validation studies, and antimicrobial resistance considerations recently highlighted in the wound-infection literature apply directly to any nanoscale antimicrobial carrier, active or passive, not yet validated against a clinically representative biofilm [28]. Reviews of gene and growth-factor delivery systems for diabetic wounds make a parallel point about payload stability: the same targeted mechanisms that improve delivery efficiency also introduce formulation complexity that has slowed clinical translation of even passive nanoparticle-based growth-factor systems, a caution that applies with even greater force to the mechanically and chemically more complex nanorobotic platforms, which must additionally survive sterilization and storage before ever reaching a wound (Figure 2) [4].

7. Conclusion

Taken together, the evidence supports three qualifying

conclusions. First, standard wound care augmented with passive nanoparticle dressings, principally silver-based antimicrobials and nanoparticle-stabilized growth factors, already has meaningful randomized trial support for incremental improvements over bare conventional dressings, and this evidence base, however modest in effect size, is the appropriate clinical benchmark against which any newer technology should be measured, rather than an untested placeholder [12,13,18]. Second, actively propelled and logic-gated nanorobotic platforms report preclinical delivery-efficiency and targeting advantages mechanistically larger than anything passive dressings have achieved, paralleling the pattern documented in oncology drug delivery, but demonstrated almost entirely outside the chronic-wound setting, in tumor, thrombosis, and generic infection models rather than in wound-specific studies [8,19,5]. Third, the absence of a trial directly comparing an actively targeted nanorobotic wound therapeutic against standard care means any claim of clinical superiority for nanorobotics in chronic wounds is, at present, an extrapolation from adjacent fields rather than a wound-specific finding, a distinction this review has tried to keep explicit throughout. The field's near-term opportunity is therefore not a more elaborate propulsion or logic mechanism, but a deliberate effort to carry the strongest existing nanorobotic and nanoparticle-based wound platforms into randomized comparison with standard care and its silver- or growth-factor-augmented variants, using the same wound-area-reduction, closure-time, and bioburden endpoints already validated in the standard-care trial literature [1,16,17].

Nanorobotic drug delivery for chronic wounds has produced a compelling mechanistic case, built on active navigation and triggered release validated in oncology and gastrointestinal delivery, and a growing set of preclinical demonstrations of targeted payload delivery and biofilm penetration that exceed what passive nanoparticle dressings achieve in comparable models [8,19,5]. Standard wound care, together with its silver- and

growth-factor-based nanoparticle extensions, carries a substantially larger and more directly comparable base of randomized trial evidence showing real, if incremental, benefit over bare conventional dressings [12,13,16,18]. Because no study has placed an actively targeted nanorobotic platform in head-to-head comparison with standard chronic-wound care, nanorobotic delivery remains mechanistically promising but clinically unproven in this indication; the most valuable next step for the field is a randomized trial designed on exactly the terms that already support standard care's passive nanoparticle extensions, rather than a further refinement of propulsion mechanism alone.

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9. Funding

This review received no external funding.

10. Conflict of Interest

The authors declare no conflict of interest.

11. Author Contributions

Wang L conceived the review and drafted the manuscript. Wu J performed the literature synthesis and prepared the figures and tables. Zhou M critically revised the manuscript for content. All authors read and approved the final version.

12. Ethics Statement

This review synthesizes previously published preclinical and clinical data and did not involve new studies on human participants or animals.

13. Data Availability

No new data were generated for this review. All sources synthesized are cited in the reference list.

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