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Review

Evolution of Thread Lifting: Advancing Toward Bioactive Polymers and Sustained Hyaluronic Acid Delivery

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Abstract: Facial aging is a multifactorial and stratified biological process characterized by progressive morphological and biochemical alterations affecting both cutaneous (Layer I) and subcutaneous (Layer II) tissues. These age-related changes manifest clinically as volume depletion, tissue ptosis, and a decline in overall skin quality. In response to these phenomena, thread lifting techniques have evolved significantly—from simple mechanical suspension methods to sophisticated bioactive platforms. Contemporary threads now incorporate biocompatible polymers and hyaluronic acid (HA), aiming not only to reposition soft tissues but also to promote dermal regeneration. This review provides a comprehensive classification and critical assessment of thread lifting materials, focusing on their chemical composition, mechanical performance, degradation kinetics, and biostimulatory potential. Particular emphasis has been given to the surface integration of HA into monofilament threads, especially with the emergence of advanced delivery systems such as NAMICA, which facilitate sustained HA release. Advanced thread materials, especially those fabricated from poly(L-lactide-co-ε-caprolactone) [P(LA/CL)], demonstrate both tensile support and regenerative efficacy. Emerging HA-covered threads exhibit synergistic bioactivity, stimulating skin remodeling. NAMICA technology represents an advancement in the field, in which HA is encapsulated within biodegradable polymer fibers to enable gradual release and enhanced dermal integration. Nonetheless, well-designed human studies are still needed to substantiate its therapeutic efficacy. Consequently, the paradigm of thread lifting is shifting from purely mechanical interventions toward biologically active systems that promote comprehensive ECM regeneration. The integration of HA into resorbable threads, especially when combined with sustained-release technologies, represents a meaningful innovation in aesthetic dermatology, meriting further preclinical and clinical evaluation.

Keywords: biorevitalization; non-surgical facelift; hyaluronic acid; skin remodeling; lifting threads

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1. Introduction

The condition of the skin serves not only as a biological interface with the external environment but also as a visible indicator of systemic health and chronological aging. As the most perceptible organ of the human body, skin quality is closely associated with self-perceived attractiveness, psychological well-being, and broader social and interpersonal dynamics. Consequently, preserving its morphofunctional integrity and mitigating age-related degradation are essential goals in both clinical dermatology and aesthetic medicine [1].

To meet these goals, a broad array of facial rejuvenation strategies has been developed beyond thread lifting. Laser-based modalities, including ablative systems such as carbon

dioxide and erbium: YAG lasers, remain central for improving photoaged skin, atrophic scarring, and dermal textural irregularities, albeit with potential downtime and risks. Less invasive light-based therapies now offer multi-wavelength versatility with reduced morbidity [2]. Photodynamic photorejuvenation combines a topical photosensitizer with targeted light activation, effectively addressing both vascular and pigmentary manifestations of photodamage while stimulating dermal remodeling [3]. Similarly, low-level light therapy with light-emitting diodes (LEDs) has demonstrated biomodulatory effects on mitochondrial function, promoting collagen synthesis and smoothing skin texture with minimal adverse effects [4]. Injectable dermal fillers, including hyaluronic acid, polylactic acid, and calcium hydroxylapatite, serve to restore volume and contour with immediate aesthetic impact and low invasiveness [5]. Chemical peeling techniques, ranging from superficial to deep, induce controlled epidermal and dermal injury to promote regeneration, increase epidermal thickness, and target pigmentary or textural skin irregularities [6]. Mesotherapy introduces bioactive compounds intradermally to improve hydration, nutrient delivery, and skin tone, whereas injectable lipolysis provides localized fat reduction for refined facial contouring [7]. Together, these modalities represent a customizable and synergistic toolkit that complements thread-based interventions in achieving comprehensive facial rejuvenation.

Thread lifting technologies have emerged as a minimally invasive yet biologically active approach for aesthetic correction. Originally developed for mechanical tissue suspension, modern thread systems now serve as multifunctional platforms that integrate structural support with regenerative signaling. By leveraging advances in polymer chemistry, bioresorbable scaffolds, and hyaluronic acid (HA) delivery, next-generation threads are designed to modulate dermal remodeling while providing immediate lifting effects.

This review aims to synthesize anatomical, histological, molecular, and materials science research related to facial aging, with a particular focus on Layers I and II. It offers a comprehensive classification of thread lifting materials and critically evaluates the regenerative potential of HA-integrated implants, especially those employing advanced encapsulation technologies such as NAMICA, for sustained dermal bioactivation.

2. Materials and Methods

A literature review was performed through a manual search of peer-reviewed publications retrieved from major scientific databases, including Scopus, Web of Science, PubMed, and the Russian Science Citation Index (eLIBRARY.RU). The search strategy utilized a range of targeted keywords relevant to the study's scope, such as facial aging, skin aging, dermal aging, cutaneous aging, extracellular matrix remodeling, dermal remodeling, hyaluronic acid in the skin, biorevitalization threads, thread lifting technology, nonabsorbable lifting threads, absorbable lifting threads, P(LA/CL) threads, HA-integrated thread implants, NAMICA thread technology, hyaluronic acid encapsulation, gradual release of HA in the skin, and noninvasive facial rejuvenation. In the case of Google Scholar, ResearchGate, and eLIBRARY. RU, search terms were applied individually.

This narrative review focused specifically on the literature addressing the clinical and experimental use of resorbable thread implants and the role of HA integration in aesthetic dermatologic procedures. Eligible publications were restricted to studies published in English or Russian within the last 15 years and included both preclinical and clinical investigations, with the exception of two sources published in 1978 and 1994, which were included individually to reflect historical aspects of the topic. No automation tools were employed in the data collection, and the review process was conducted manually. This review was not formally registered, and no predefined protocol was established.

3. Results

3.1. Types of Threads and the Materials They Are Made of

Modern thread lifting techniques for correcting age-related facial changes have evolved through continuous advancements in thread composition and clinical protocols. Recent progress in tissue engineering, regenerative medicine, and biocompatible materials has provided a robust scientific foundation for integrating innovative thread technologies into dermatological practice, thereby broadening the therapeutic options in aesthetic medicine.

Modern lifting threads are systematically classified on the basis of a number of parameters that determine their biomedical and operational properties. The key classification criteria include the chemical nature and biodegradation characteristics of the material, morphometric parameters (including diameter), mechanical strength, and microstructure and surface topography, which influence tissue integration and the degree of fibrous response. The functional features of the threads also play an important role in the selection of a specific technique and in determining the expected clinical outcomes when performing thread lifting procedures [8].

Notably, the structural component of thread implants plays a critical role in modulating the biological responses of recipient tissues, determining the degree of biocompatibility, the characteristics of the inflammatory reaction, and the extent of neocollagenesis and angiogenesis. Furthermore, the structural features of a material largely determine its susceptibility to microbial adhesion and subsequent bacterial colonization [9].

Lifting threads are classified on the basis of their surface morphology and physical properties. An example of such a classification is presented below [8] (Figure 1):

- Monofilament (Mono) sutures are smooth-surfaced threads designed to minimize tissue trauma during insertion. They are most often used for reinforcement. These threads are quite thin and are therefore ideal for working with delicate areas, such as thin skin and regions with minimal subcutaneous fat. Their primary function is to stimulate the formation of a collagen framework in the dermis and to improve skin quality by inducing microtrauma in the tissues.
- Spring/Twin threads are a type of thread implant characterized by pronounced elastomeric properties, including “shape memory” capabilities. After implantation into tissues, they tend to return to their original helical configuration, providing a pronounced mechanical lifting effect through the distribution of tension vectors within the three-dimensional structure of the dermis and hypodermis. This design feature helps not only in repositioning soft tissues but also in effectively correcting local asymmetry, shaping desired contours, and restoring lost volume in areas affected by age-related involution.
- Barbed sutures, featuring barbed structures along the entire length of the thread, provide mechanical fixation within the SMAS layer, contributing to the formation of a stable tension vector and a prolonged lifting effect. The morphology of the barbs varies depending on the clinical task and the intended area of correction. Currently, designs with unidirectional, bidirectional, or multidirectional barb orientation are used, depending on the clinical task and the intended area of correction. These modifications optimize the tension distribution, achieve uniform tissue traction along the implantation line, and minimize the risk of displacement. Thus, barbed sutures combine a mechanical lifting effect with the biostimulating potential associated with the tissue response to microtrauma, making them a highly effective modality for the aesthetic correction of age-related changes.

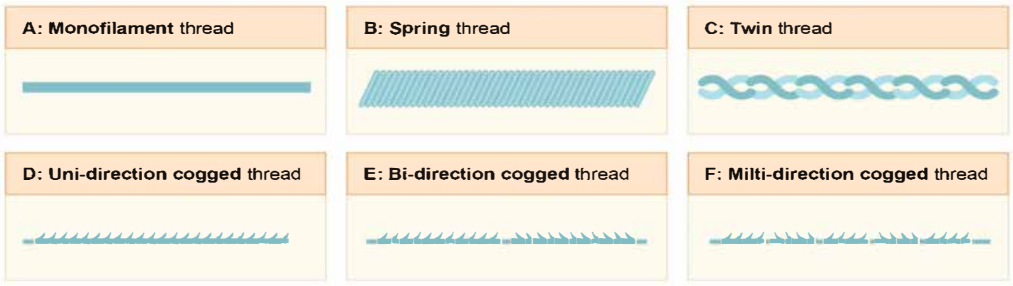


Figure 1. Types of lifting threads by morphological characteristics.

The dimensional characteristics of suture materials are regulated by international pharmacopeial standards, among which the classifications proposed by the United States Pharmacopeia (USP) and the European Pharmacopoeia (EP) are the most widely used. In practice, the USP system is predominantly used, providing a unified approach to thread gauge designation [8].

According to this system, the size of the suture material is encoded via a pair of Arabic numerals, where the first digit indicates the gauge number, and the "0" following the slash (e.g., 2/0, 3/0) denotes inclusion in the subzero series; the higher the first digit is, the smaller the thread diameter. Thus, a 3/0 thread (pronounced "three-zero") has a smaller diameter than a 2/0 thread ("two-zero"), with the material of composition not considered in this classification (Figure 2).

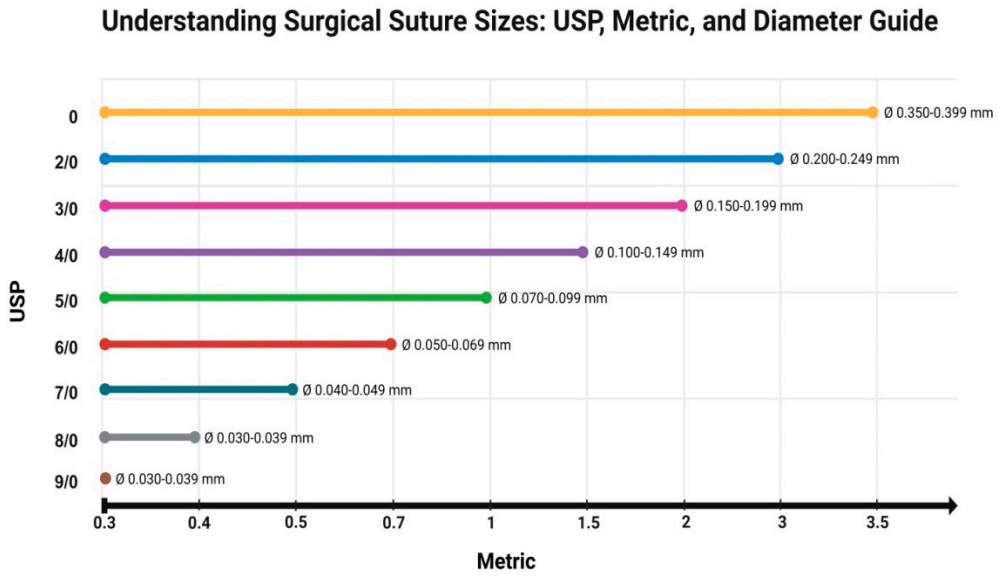


Figure 2. Illustrative diagram of suture sizes.

This standardization of suture calibers ensures reproducibility in clinical practice; facilitates precise thread selection on the basis of the anatomical region, tissue characteristics, and extent of the intended intervention; and serves as a guideline for rational choice in specific surgical and aesthetic procedures.

When implanted in soft tissues, a lifting thread is generally capable of inducing three distinct rejuvenating effects: lifting, reinforcing, and biostimulating. Clinical observations indicate that each specific type of thread tends to predominantly exhibit one of these effects, whereas the other two types are present to a lesser extent [10,11].

As noted earlier, certain types of lifting threads are characterized by the presence of specialized fixation elements on the thread surface, including notches, "teeth", cones, or dents. These textural structures play a critical role in anchoring tissues, preventing retraction to their original position, and thereby providing a stable lifting effect.

Typically, threads of size 1/0 or 2/0 according to the USP classification are used for such purposes and possess the high mechanical strength necessary for stable traction and for withstanding the mechanical load generated by tissue forces.

Notably, when placed without displacement of soft tissues, the functional role of such threads is limited to passive stabilization of the skin-muscle framework, which serves primarily as a reinforcing rather than a traction tool [12].

Reinforcing threads are implants designed for internal stabilization of soft tissue structures and the creation of a supportive dermal framework that promotes ECM remodeling. Their primary mechanism of action occurs through the stimulation of regenerative processes in response to microtrauma rather than through tissue displacement, as observed with lifting threads.

A key advantage of reinforcing threads is the bidirectional orientation of textural elements, which ensures self-anchoring of the implant without the need for a separate fixation point. The absence of a local stress zone that experiences excessive loading from displaced tissues reduces the risk of side effects. The arrangement of the textural elements can be mirror-symmetrical or alternating, allowing for individualization of the implantation technique tailored to the anatomical and functional characteristics of the correction area [12].

Biostimulating threads are a type of implantable suture material whose primary mechanism of action occurs not through mechanical means but through the activation of tissue regeneration processes. Their biological activity is attributed primarily to their chemical composition and the physiological response of tissues to the implantation of a foreign material, leading to an inflammatory reaction and subsequent remodeling. As a result, stimulation of neocollagenesis and an increase in the density of the dermal matrix are observed around the implanted threads [12–14].

Despite their pronounced biostimulating potential, these threads have minimal or no ability to produce lifting or structural support effects, thereby limiting their application solely to enhancing skin quality, including improvements in turgor, texture, and microrelief.

As a rule, biostimulating threads have a small diameter (up to 3/0 according to the USP classification), are highly flexible, and are produced in either smooth or textured forms. The choice of surface type depends on the clinical task: smooth threads are mainly used in delicate facial areas, whereas textured threads are employed to enhance the tissue response owing to their increased surface area for interaction with surrounding structures and stronger fixation [12].

Lifting threads can be classified as nonabsorbable (polypropylene, silicone, silicone-coated polyester, polyester (polyethylene terephthalate—PET), and medical-grade silicone) or absorbable (polydioxanone (PDO), poly-L-lactic acid (PLLA), polycaprolactone (PCL), poly(lactic-co-glycolic acid) (PLGA), P(LA/CL), and P(LA/CL)-HA) [8]. Nonabsorbable threads are characterized by high durability and resistance to degradation by biological tissues. In contrast, absorbable threads have lower tensile strength and are designed to be completely absorbed over time with minimal or no tissue reactions. The resorption rate of these threads varies within specific timeframes and depends on the material selected or the product brand [15].

As previously stated, lifting threads are manufactured from various materials on the basis of their unique properties and areas of application. This selection aligns with surgical objectives and patient needs, considering the desired durability and tissue interaction.

Polypropylene, a nonpolar, partially crystalline thermoplastic and nonabsorbable polymer, is widely used in medical practice. It is valuable in procedures aimed at achieving long-term effects because of its low tissue reactivity, very low coefficient of friction, and resistance to biodegradation [16,17]. Its high tensile strength underpins its clinical significance in aesthetic correction protocols, specifically for correcting morphological

manifestations of chronological aging, such as blurring of the jawline, deep nasolabial folds, and ptosis in the malar region [18].

Furthermore, utilizing these properties, APTOS LLC (Tbilisi, Georgia) has developed an original minimally invasive technique focused on correcting facial asymmetry resulting from peripheral facial nerve paresis. The proposed protocol involves topographically guided insertion of polypropylene threads into the subcutaneous layer, considering the individual anatomical and functional characteristics of the affected and intact sides [17].

Silicone threads, resembling elastic bands, represent a distinct class of nonabsorbable implants, differing from traditional suture materials in both composition and functional purpose. The main clinical application of these threads involves surgical interventions requiring dynamic movement, changes in topography, rotation of soft tissues, or temporary fixation of anatomical structures. The implantation of a silicone suture involves its passage through designated tissue layers, targeted positioning, and subsequent reliable fixation. Owing to its high elasticity, the material allows for secondary adjustment; if tension weakens, the thread's position can be readjusted without requiring complete revision of the implantation area [19]. Silicone threads are widely used in pelvic floor reconstructive surgery, particularly in vaginoplasty and prolapse correction, where their elasticity accommodates the physiological mobility of tissues and the patient's anatomical features [20].

Despite the active development of biodegradable thread technologies, nonabsorbable threads still retain clinical importance in certain cases of aesthetic and reconstructive surgery. However, the high risk of long-term consequences associated with their use is increasingly prompting revisions of therapeutic strategies in favor of absorbable thread implants, which offer a more favorable safety and biocompatibility profile [21].

The key limitation of nonabsorbable threads is their permanent presence in tissues, leading to a prolonged inflammatory response through chronic stimulation of foreign body responses. At the histological level, this can be accompanied by granuloma formation, the development of a pronounced fibrous sheath, and fibrous transformation of surrounding structures, particularly in patients with a predisposition to excessive fibroblast proliferation [20].

Aesthetically, these threads are often associated with the risk of visible defects, such as skin retraction at the site of thread passage, contouring, or palpability of the implant, which are especially pronounced during age-related involution of layer II of the facial region [22].

PDO threads are synthetic, biodegradable, and fully absorbable polymers characterized by high biocompatibility and a well-established safety profile. The material degrades through hydrolytic cleavage, with complete metabolic elimination of the threads typically completed within six months after implantation. In their smooth (monofilament) form, PDO implants do not exert traction effects but effectively stimulate neocollagenesis through microtrauma and fibroblast activation. This makes them particularly effective in correcting static wrinkles and generally improving skin quality [13,23,24]. Surface modifications of PDO threads, including the creation of textured structures (e.g., notches, barbs, "teeth", and spiral twisting), significantly increase their fixation capacity and provide mechanical support to soft tissues. Owing to the optimal combination of biostimulating and structural-mechanical effects, PDO threads in various configurations occupy an important place in modern thread rejuvenation protocols [25–27].

After PDO thread implantation, a cascade of processes aimed at tissue remodeling and improving the morphological and functional state of the skin is initiated. The primary mechanism of PDO threads is the activation of neocollagenesis and fibrillogenesis, accompanied by gradual contraction and restructuring of the fibrotic dermis. This leads to moderate skin retraction, improved skin tone, and a visual lifting effect [28,29].

At the histological level, the increase in density and thickness of the dermal matrix, along with stimulation of neovascularization, contributes to increased tissue trophism

and normalization of microcirculation. Moreover, partial denaturation of the adipocytic deposits involved in volume formation is observed, which may contribute to gentle contour correction and lifting without excessive volume creation [24,29].

Additionally, PDO threads induce the formation of granulation tissue, indicating the onset of the early phase of the reparative response. This stage involves not only the production of new collagen matrices but also their integration with existing fibrillar structures in the dermis. This architectural reorganization of the skin matrix contributes to improved elasticity, density, and homogeneity of the skin, providing a natural and aesthetically pleasing restoration of skin texture and contours [30].

Despite its benefits, PDO thread technology has notable limitations. Its short biodegradation cycle—about six months—may be insufficient for forming a lasting connective tissue framework. Additionally, its nonspecific and unstructured stimulation of neocollagenesis, particularly with superficial thread implantation or in cases of thin dermis, can lead to local fibrosis, thread contouring, and the formation of aesthetically significant irregularities and microdeformations. As a softer, less durable material than the PLLA or PCL, the PDO is less suitable for individuals with significant tissue density, gravitational ptosis, or excess subcutaneous fat. Without supplementary treatments, outcomes may be unstable, particularly in older patients with advanced aging changes [22,24,31].

PLLA is a biocompatible, biodegradable, and absorbable synthetic polymer widely used in aesthetic medicine, both as a component of injectable volumizers and as a material for thread lifting technologies aimed at restoring volume and correcting age-related soft tissue ptosis and deformation [32].

Following implantation, PLLA threads undergo hydrolytic de-esterification, resulting in the breakdown of the polymer into lactic acid monomers. These metabolites are subsequently metabolized via the tricarboxylic acid (Krebs) cycle, are ultimately converted into carbon dioxide and water, and are completely eliminated from the body. The complete biodegradation cycle of PLLA averages 16–18 months and may last up to 24 months, significantly exceeding the resorption period of PDO-based threads [8,33,34].

This type of thread operates via a dual mechanism: providing immediate mechanical lifting and a delayed biostimulating effect by triggering regenerative processes. Following implantation, a mild inflammatory response initiates neocollagenesis, activating fibroblasts and promoting type I and III collagen synthesis to strengthen the dermal matrix [32,35]. Over approximately 24 months, PLLA has been gradually replaced by new collagen, supporting tissue remodeling and improving aesthetic results [36].

PLGA is a biocompatible, biodegradable copolymer of polylactic acid (PLA) and polyglycolic acid (PGA) that is known for its structural stability, which lasts up to 24 months post-implantation. Its combination of mechanical strength and controlled resorption makes it ideal for long-acting threads used in minimally invasive facial lifting. PLGA threads enable immediate mechanical lifting as well as delayed soft tissue remodeling by stimulating the synthesis of fiber-forming components of the ECM, effectively addressing gravitational ptosis, reduced skin turgor, and age-related facial contour changes [8].

As noted earlier, a key advantage of these materials over PDO is their delayed biodegradation, which allows for prolonged maintenance of the mechanical lifting effect after the procedure. This is due to the high stability of the polymer structure in recipient tissues, making PLLA and PLGA threads preferable for the long-term support of soft tissue structures. However, the biostimulating effect of these threads, particularly the induction of neocollagenesis, does not manifest immediately after implantation but rather occurs with a delay as part of the late reparative response [8,34,37].

PCL is a biocompatible, biodegradable polymer valued for its elasticity and resistance to mechanical stress, making it well-suited for aesthetic dermatology. Compared with the

PDO and PLLA, the PCL offers greater flexibility and elasticity, reducing patient discomfort during and after implantation [38,39]. It degrades gradually over 12–18 months into inert byproducts, water, and carbon dioxide, which are completely eliminated from the body through natural metabolic pathways [38,40]. This prolonged resorption ensures prolonged tissue support as well as a sustained biostimulating effect in terms of structural remodeling of the dermis. Clinical studies have demonstrated that PCL-based threads have a superior capacity to induce collagen synthesis than do PDO- and PLLA-based materials. This primarily stimulates the production of type III collagen, leading to a decrease in the collagen I/III index, improving skin elasticity and enabling more physiological tissue restructuring, especially in age groups characterized by pronounced involutional changes [39,41,42].

Notably, similar to PLLA and PLGA threads, collagenogenesis with PCL threads occurs with a delay. The biological response gradually progresses, with initial signs of skin remodeling becoming evident several weeks after the procedure [39].

P(LA/CL), a copolymer obtained through ring-opening polymerization of L-lactide and ε-caprolactone, is a highly effective biomaterial with proven biocompatibility, safety, and high tissue tolerance, rendering it promising for use in minimally invasive aesthetic procedures, including thread lifting techniques [43]. After implantation into biological tissues, the material undergoes stepwise degradation, initially degrading into individual components—polylactide and polycaprolactone—which are subsequently hydrolyzed to lactic and 6-hydroxycaproic acids, respectively. These products are metabolized via natural metabolic processes and are completely eliminated from the body [44].

According to experimental studies, complete biodegradation of P(LA/CL) occurs within approximately 24 months, owing to its slower resorption rate than that of other biodegradable copolymers, resulting in prolonged support and stable fixation of soft tissue structures [17,45].

P(LA/CL)-based threads provide both immediate lifting and long-term biostimulation due to their balanced composition, with 25% ε-caprolactone increasing the strength, elasticity, and degradation time. This composition also promotes lactic acid diffusion, stimulating fibroblasts, neocollagenesis, and elastin synthesis. Histologically, these threads remodel the dermal matrix, improve skin architecture, and form a stable connective framework, delivering lasting rejuvenation, which is particularly effective in areas with ptosis and volume loss [17,46,47].

In aesthetic medicine, resorbable sutures are widely used for immediate mechanical lifting by repositioning soft tissues, with their gradual degradation supporting long-term tissue remodeling. While current thread designs already offer high mechanical performance, further improvements provide limited clinical benefit. As a result, the focus has increasingly shifted toward their biorevitalizing potential—particularly their capacity to stimulate cellular activity and matrix remodeling—marking a promising direction for future innovation and research.

3.2. Function of Hyaluronan in Cutaneous Wound Repair

GAGs represent some of the most complex polysaccharides of the ECM and play crucial roles both in maintaining tissue homeostasis and in the development of various pathological processes [48,49]. HA, a nonsulfated GAG composed of disaccharide units of glucuronic acid and N-acetylglucosamine, is one of the key members of this group. Owing to its unique structure and biological properties, HA plays an important role in the structural and functional organization of the ECM [50].

These data indicate that HA has a molecular weight-dependent influence on cell behavior, including parameters of proliferation, migration, and angiogenesis. Low-molecular-weight fractions of HA within the molecular weight (MW) range of 400–10,000 Da exhibit

pronounced proangiogenic activity, whereas fragments ranging from 50,000 to 100,000 Da predominantly stimulate cell migration and increase proliferation rates. In contrast, high-molecular-weight HA (HMW-HA) (MW > 500,000 Da) inhibits angiogenesis, restricts cell migration, and reduces proliferative activity, acting as a functional antagonist of short-chain forms. Moreover, fractions with MW > 1,000,000 Da demonstrate pronounced anti-inflammatory effects and possess high hydrating capacity. Therefore, to achieve specific biological effects in tissue engineering and regenerative medicine, HA fractions with precisely controlled molecular weights are used to ensure specific modulation of the cellular response [51–56].

The process of skin wound healing is complex, initiated by the disruption of skin integrity, and involves various cellular activities across distinct phases. These phases include the initial inflammatory stage, followed by the proliferative or tissue repair stage, and culminate in the remodeling stage. Throughout these stages, HA assumes specific roles, contributing significantly to the regulation and progression of wound healing [57]. These findings underscore the importance of HA and other GAGs in maintaining not only structural integrity but also the functional efficacy of tissue repair mechanisms.

During the inflammatory phase of wound healing, HA levels sharply increase, peak at approximately 3 days post-injury, and then decrease, as was initially documented in research conducted by Dunphy J.E. [58]. This surge is driven primarily by platelets, megakaryocytes [59], and keratinocytes via upregulated HA synthase genes (Has2, Has3) [60,61]. The resulting accumulation of HMW-HA promotes water diffusion and edema, facilitating immune cell infiltration while also exerting anti-inflammatory effects and reducing vascular leakiness, thus supporting early wound healing [53,62].

During the proliferative phase of wound healing, HA regulates key cellular functions by promoting fibroblast migration [63], preventing apoptosis [64,65], and supporting their transformation into myofibroblasts [63]. It also aids in the formation of new tissue scaffolds to reinforce the structural matrix [63]. Additionally, HMW-HA inhibits angiogenesis by limiting endothelial cell proliferation and disrupting their monolayer [66], thereby impeding intercellular communication [67].

Normal wound healing leads to scar formation through coordinated interactions between fibroblasts and the ECM, with collagen turnover being balanced at approximately three weeks post-injury. As healing progresses, HA and other wound-specific elements are degraded and replaced by an avascular, collagen-rich scar [68]. Meyer L.J.M. and Stern R. reported that HA remains consistently present in the upper dermis from fetal development through old age [69]. However, its extractability varies due to differing levels of hyaladherin binding, influencing its functional role in scarring. Additionally, Balaji S. et al. demonstrated that treatment with HA and IL-10 can induce adult fibroblasts to adopt fetal-like characteristics, emphasizing the regulatory role of HA in fibroblast activity and scar formation [70].

3.3. Hyaluronic Acid: Clinical Application in Aesthetic Medicine and Synergy with Thread Technologies

The pronounced dermatotropic properties of HA, combined with its ability to regulate the viscoelastic characteristics of the skin, underpin its extensive application in aesthetic medicine for the management of age-related changes. In addition to their cosmetological use, HA-based biomaterials have gained prominence in regenerative medicine as promising agents for promoting reparative processes and facilitating tissue function restoration because of their high biocompatibility and capacity for structured three-dimensional matrix formation. This versatility highlights the critical role of HA in both aesthetic and clinical contexts of contemporary medical practice [71].

A decrease in HA content within the ECM, coupled with diminished hydrophilicity, results in compromised skin hydration, reduced elasticity, and disruption of tissue microarchitecture, ultimately contributing to dryness and cutaneous laxity. Accordingly, most antiaging therapeutic strategies are directed toward mitigating these alterations [72].

The efficacy of HA-based products in addressing age-associated changes has been demonstrated in multiple clinical and experimental studies. The formulations investigated include various delivery systems, such as serum [73,74], creams [54,75], dermal fillers [76,77], subdermal fillers [78], gels [79,80], and thread-based systems [81,82].

Biorevitalization via both single-component and combined HA-based formulations is a well-established mesotherapeutic approach for correcting age-related skin changes by restoring the ECM structure and creating favorable conditions for optimizing skin cell metabolism. However, it is insufficient to address age-related loss of facial soft tissue volume on its own and must be integrated with other antiaging strategies for comprehensive results. In this context, dermal fillers based on stabilized (cross-linked) HA have been a cornerstone of aesthetic medicine for decades because of their effectiveness in restoring volume in areas affected by wrinkles, folds, lipodystrophy, and localized skin defects resulting from surgical interventions or traumatic injuries—conditions classified as "tissue loss" states [72].

Ten years ago, the primary application of HA-based dermal fillers was the localized correction of age-related changes in facial skin, primarily through the smoothing of linear wrinkles and folds. However, in recent years, aesthetic medicine has undergone a distinct shift from isolated injections to more comprehensive three-dimensional facial contouring strategies involving the simultaneous treatment of multiple anatomical areas. Modern techniques involve the injection of fillers into deeper layers of soft tissue, resulting in marked and durable aesthetic outcomes [83,84].

In parallel with the development of volumetric injection techniques, promising findings regarding the use of HA in the form of thread-based systems have been reported in the scientific literature [81]. In vivo studies have confirmed the effectiveness of pure HA threads, demonstrating their ability to induce neocollagenesis with a minimal inflammatory response. Moreover, compared with traditionally utilized resorbable threads based on PDO, HA threads presented higher expression levels of type III collagen and a statistically significant increase in transforming growth factor beta-1 (TGF-β1), surpassing the levels observed with standard HA fillers [82].

Despite the wide variety of available HA formulations, detailing their individual advantages and limitations is beyond the scope of this work. Nevertheless, it is important to emphasize that, to date, none of the existing cosmetic modifications of HA fully meet all aesthetic requirements. Since no single treatment approach can safely and effectively address age-related changes across all anatomical areas of the face, consensus guidelines for facial rejuvenation have been developed within the professional community. These studies recommend an integrated, multitechnique approach, individualized according to the morphological and functional characteristics of each facial area. This strategy significantly enhances both the safety and overall effectiveness of aesthetic interventions [85].

Aesthetic medicine currently shows a consistent trend toward integrating both surgical and nonsurgical methods to restore a youthful and harmonious appearance. Within this consensus approach, particular emphasis is placed on the combined use of HA-based dermal fillers and thread lifting as key nonsurgical strategies for addressing age-related changes [86]. Fillers containing stabilized HA demonstrate high clinical efficacy by enabling facial contouring, minimizing wrinkles, increasing skin hydration, and compensating for soft tissue volume loss [72,87]. In contrast, thread lifting involves inserting threads into the

subcutaneous layers to mechanically elevate tissues and redefine facial contours [88] while also stimulating neocollagenesis to increase skin firmness and elasticity [13].

Given the complementary advantages of these techniques, clinical protocols that integrate their combined use have been developed in aesthetic medicine. The integration of HA-based fillers and thread lifting enables more precise customization of corrective procedures to the patient's individual anatomical and age-related characteristics. However, despite considerable clinical interest, published data on this topic remain limited: currently, only a small number of scientific publications and clinical reports are available that provide a detailed analysis of the outcomes associated with this approach [85,86,89–94].

Notably, the aesthetic effect achieved with HA-based dermal fillers is temporary and necessitates regular maintenance injections [95]. These interventions, along with thread lifting, constitute additional invasive procedures, which, in certain cases, may raise concerns regarding the rationality and justification of such an approach.

Within the framework of the described synergistic approach, a third generation of thread implants has been developed, characterized by the integration of biodegradable polymer fibers with active biological agents, particularly HA. This combination not only preserves the traditional role of threads as a fixation framework but also exerts a biorevitalizing effect on the skin, making these systems particularly promising for comprehensive skin rejuvenation strategies.

Modern P(LA/CL)-based thread implants modified with HA represent a novel solution in the field of minimally invasive aesthetic correction, combining mechanical lifting with biorevitalization. Owing to the synergistic combination of structural support and dermal remodeling, these threads demonstrate a comprehensive therapeutic effect, targeting both facial contour correction and improving the morphological and functional condition of the skin [17,47].

The integration of HA contributes not only to increasing effects through additional tissue tension and moisture fixation but also to stimulating cellular activity, including fibroblast proliferation and the synthesis of ECM components. This results in gradual dermal remodeling, improving the skin texture, hydration, and elasticity during the post-procedure period [96,97].

Clinical evidence indicates that incorporating HA into thread systems enhances reparative processes, reduces inflammation, and shortens recovery time, thereby improving patient satisfaction and expanding outpatient applications [98,99]. P(LA/CL)-HA threads represent a significant advancement in minimally invasive rejuvenation by combining mechanical lifting with biorevitalization, resulting in both immediate contouring and sustained skin regeneration [17,47]. Reflecting broader trends in aesthetic medicine, thread technologies have shifted from purely mechanical tools to multifunctional systems that support long-term dermal remodeling. Central to this evolution is the integration of biodegradable polymers with medium- and HMW-HA, which play key roles in tissue hydration, fibroblast stimulation, and ECM stabilization.

From a scientific and technological perspective, a promising direction for the further development of thread implants is the improvement of the gradual release of biorevitalizing agents. Particular attention in this context should focus on two main objectives: first, minimizing the issue of "burst release," which refers to the premature and excessive release of HA from the thread surface; second, developing a system for the prolonged release of HA, aligned with the biodegradation kinetics of the polymer matrix.

Methods to protect non-cross-linked HA, an endogenous polysaccharide physiologically identical to components of the human ECM, have attracted particular attention. In its native form, HA has high solubility, low viscosity, insufficient mechanical strength, and

rapid biodegradation in vivo, all of which significantly limit its practical application in various biomedical fields [100].

To enhance the functional properties of HA, such as viscosity, mechanical strength, resistance to enzymatic degradation, and biological activity, various approaches to its chemical modification and cross-linking via different chemical agents have been developed [101,102]. As a result, since the mid-1990s, the chemically stabilized form of HA has gained widespread use in aesthetic medicine as a base material for dermal fillers intended for the correction of age-related skin changes [103]. Today, cross-linked HA occupies a substantial share of the injectable aesthetic medicine market [102].

The use of stabilized HA in dermal fillers is considered justified, as the non-cross-linked form is characterized by low viscosity, limited mechanical stability, and rapid clearance from the injection site within a few days. This is due to the extremely short residence time of native HA molecules in the skin, where they undergo rapid degradation under the influence of endogenous factors, such as hyaluronidase and reactive oxygen species. These agents initiate fragmentation of the polymer chains, significantly accelerating the biodegradation of HA. On average, the half-life of non-cross-linked HA in tissues is approximately 1–2 days, after which the molecules disperse into the aqueous phase and subsequently undergo enzymatic cleavage in the liver, resulting in the formation of final metabolic products—water and carbon dioxide [100].

However, despite the superior mechanical and biological properties of cross-linked HA, concerns have been raised regarding the presence of chemical cross-linking agents, which may exhibit cytotoxic effects depending on their chemical nature [104–106]. In this context, to achieve a pronounced biorevitalizing effect, the use of non-cross-linked HA is preferable, provided that an effective delivery system, such as nano- or microsphere encapsulation or hydrogel matrices, is in place to protect the molecules from premature enzymatic degradation and prolong their activity in tissues.

Modifying technological approaches to the production of next-generation thread implants, considering these aspects, would help achieve a consistent remodeling effect over time, contributing to a gradual and sustained improvement in the morphological and functional characteristics of the skin.

Although HA-coated threads exhibit exceptional biocompatibility and regenerative capabilities, their development has historically been constrained by several technical barriers. These include their inherent susceptibility to rapid enzymatic degradation, the challenge of preserving sufficient tensile strength, and limitations in scalable manufacturing processes. Consequently, the clinical application of HA-based threads has remained limited despite their significant therapeutic potential.

Since 2019, however, APTOS LLC has initiated a focused and collaborative research and development program aimed at overcoming these limitations. In partnership with specialized laboratories, including those with expertise in electromechanical engineering, the company has successfully established dedicated manufacturing infrastructure—comprising precision-engineered equipment, fully equipped laboratories, and certified cleanroom environments—to facilitate the production of advanced HA-coated thread systems.

Through a rigorously scientific and engineering-led approach, APTOS LLC has achieved the industrial-scale manufacture of HA-coated threads that demonstrate consistent mechanical stability. These threads exhibit tensile properties on par with those of conventional uncoated copolymer sutures, such as reference suture 2/0, thereby meeting essential performance benchmarks for clinical use. Production capacity has expanded substantially, with several thousand units now being produced monthly across facilities located in Russia and Georgia.

Nonetheless, regulatory compliance—particularly in terms of securing international certifications such as CE marking and FDA approval—continues to pose significant challenges. The CE approval process is currently in progress. Importantly, the limited global availability of HA-based threads is not indicative of insufficient demand but rather reflects the sophisticated technological requirements necessary for their reliable development and mass production.

To date, APTOS LLC remains the sole company to have successfully translated this complex biotechnological innovation into a reproducible, industrial-scale product, setting a precedent in the field of bioresorbable thread technologies, especially in the case of P(LA/CL)-based thread implants.

One such approach is the encapsulation of HA via the NAMICA method, which was developed by APTOS LLC and protected by Russian Federation Patent № RU2782112C2, dated 21 October 2022 [107].

The abbreviation NAMICA (NAno–MIcro–CApsule) is based on a multiscale encapsulation principle, in which sodium hyaluronate (SH) is encapsulated within a copolymer shell either as microparticles ($\geq$1 μm) or as nanoparticles ($\leq$0.1 μm), enabling flexible control over the release kinetics of the active substance. The basic structural unit of this technology consists of a copolymer of PLLA and D-lactide (PDLA) in a 1:1 ratio, combined with non-cross-linked SH of medium molecular weight [108,109].

The coating formation process begins by mixing 2 wt% SH with 98 wt% isopropyl alcohol. This is followed by the addition of an organic solvent and a copolymer, after which a microfiber coating is applied to the surface of the threads by electrospinning for 60 s. As a result, a stable polymer matrix with polysaccharide particles encapsulated within it is formed [108].

The choice between micro- or nanoscale HA capsules depends on the initial stage of HA preparation: either microgranulation followed by application (P(LA/CL)-HA-micro) or modification and dissolution in organic solvents to obtain a nanofraction (P(LA/CL)-HA-nano).

A key factor in this context is the potential for prolonged release of HA, which is achieved through the gradual degradation of the polymer shell. High-performance liquid chromatography (HPLC) performed under phosphate-buffered saline (PBS) conditions at physiological pH (7.4) enables precise monitoring of the substance release kinetics and modeling of the drug's pharmacodynamic parameters in vitro [108,109].

Preclinical morphological investigations provide compelling evidence supporting the regenerative potential of bioactive thread implants composed of P(LA/CL) copolymers functionalized with HA. Early in vivo studies demonstrated a favorable biological response, marked by the initiation of reparative pathways and remodeling of the ECM in the treated tissue environment. These findings underscore the biorevitalizing properties of HA-encapsulated threads and emphasize the critical role of sustained HA release in mediating long-term dermal regeneration [108,109].

To build upon these initial observations, further in-depth preclinical analyses are warranted. Future research should employ advanced investigative modalities, including immunohistochemical assays, ultrastructural imaging techniques, and molecular and genomic profiling of ECM remodeling biomarkers. Proteomic analysis may further elucidate the complex biological cascades involved. Such a multidimensional approach will facilitate a more comprehensive understanding of the underlying regenerative mechanisms, offer mechanistic validation of observed histological outcomes, and establish a stronger scientific foundation for clinical translation.

The current morphological insights should directly inform the design and refinement of next-generation thread-based systems, with particular attention given to optimizing

their physicochemical properties and biofunctional performance. One promising direction involves the engineering of dual-delivery thread platforms capable of incorporating both microencapsulated HA and nanoencapsulated HA. This combined strategy has the potential to enhance the therapeutic efficacy of the implant by leveraging the complementary advantages of each delivery format while mitigating their individual limitations.

Despite the encouraging nature of these preliminary findings, the limitations of current experimental models and the absence of clinical validation must be acknowledged. Accordingly, these results should be regarded as a foundation for the development of rigorously designed human trials aimed at evaluating the safety, clinical effectiveness, and long-term outcomes of HA-functionalized thread implants in aesthetic dermatology.

4. Conclusions

Facial aging is a complex, multifactorial biological process involving progressive structural, biochemical, and cellular changes across both the cutaneous and subcutaneous tissue layers.

In parallel with advancing insights into the anatomical and molecular basis of facial aging, thread lifting technologies have undergone substantial innovation. These devices have transitioned from rudimentary mechanical lifting tools to multifunctional platforms capable of exerting both structural and regenerative effects. Thread implants composed of P(LA/CL) copolymers functionalized with HA are of particular clinical interest. These hybrid materials offer dual benefits: immediate biomechanical support and prolonged stimulation of dermal remodeling. Notably, the incorporation of controlled-release delivery systems, such as the NAMICA platform, represents a critical milestone, enabling sustained HA bioavailability and improved tissue integration.

Preclinical studies have provided robust evidence for the regenerative potential of these advanced thread systems. Initial in vivo data highlight favorable histological outcomes, including enhanced neocollagenesis and ECM reorganization, underscoring their biostimulatory efficacy. However, despite encouraging experimental findings, the translational value of these approaches is presently limited by the lack of long-term clinical trials and the intrinsic limitations of animal models. To validate the therapeutic efficacy and safety of HA-integrated threads, future research must prioritize well-designed human studies employing comprehensive, multilayered methodologies, such as immunohistochemical profiling, ultrastructural imaging, and proteogenomic analyses.

In summary, the integration of HA into biodegradable thread matrices represents a paradigm shift in the field of aesthetic dermatology. By uniting immediate mechanical lifting with sustained dermal regeneration, these next-generation implants offer a promising, minimally invasive strategy for facial rejuvenation. As this technology continues to evolve, it may play a pivotal role in the development of individualized, biomimetic interventions for age-related skin restoration.

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