https://doi.org/10.33472/AFJBS.6.2.2024.1279-1286

African Journal of Biological Sciences

Research Paper Open Access

Stapedotomy Using Hyaluronic Acid for Management of Otosclerosis

Toqa Ibrahiem Soliman Ibrahiem, Atef Taha Elbahrawy, Magdy Bedir Albaramawy, Amany Mohamed Abd Al Badea

Otolaryngology Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author : Toqa Ibrahiem Soliman Ibrahiem

Email: t0qa29elbagory@gmail.com

Article History

Volume 6, Issue 2, April 2024

Received:19 April 2024

Accepted: 15 June 2024

Published: 15 June 2024

doi: 10.33472/AFJBS.6.2.2024.1279-1286

Abstract: Otosclerosis (localized bone dysplasia) is a primary disease of the human otic (labyrinthine) capsule and stapes footplate. Depending on the site, size, and histologic features of the pathologic involved area hearing and balance are affected. When describing otosclerosis, it is important to distinguish between the histological and the clinical form of the disease. Clinical/radiological otosclerosis refers to the presence of otosclerotic foci at the site where it causes conductive hearing loss by interfering with the motion of the stapes or of the round window membrane. The main therapeutical choice is stapes surgery. However, rarely alternative surgical approaches may be required such as bone anchored implantable devices, middle ear implants or cochlear implants, based on patient conditions and the severity of hearing loss. The patient should have a PTA demonstrating a conductive or mixed hearing loss (sometimes with a Carhart's notch) with a large enough ABG and absent stapedial reflexes. The affected ear should be the worse hearing ear. Speech discrimination should be sufficient to justify the risk of the procedure. Clinical examination should exclude other middle ear disease and the tympanic membrane should be intact. Imaging can help to confirm the clinical diagnosis or exclude other pathologies.

Keywords: *Stapedotomy, Hyaluronic Acid, Otosclerosis*

Introduction

Abnormal bony growth starts in the bony labyrinth and oval window moving toward the auditory ossicles leading to conductive hearing loss. The hardening of the structures results in loss of flexibility and ultimately prevents the stapes footplate from transmitting oscillations to the oval window. The pathologic process involves new bone formation and proliferation of the vasculature. Histologically, increased osteoblasts and osteoclasts are seen with the presence of abnormal sclerotic bone **(1)**.

Otosclerosis (localized bone dysplasia) is a primary disease of the human otic (labyrinthine) capsule and stapes footplate. Depending on the site, size, and histologic features of the pathologic involved area hearing and balance are affected. When describing otosclerosis, it is important to distinguish between the histological and the clinical form of the disease **(2)**.

Clinical/radiological otosclerosis refers to the presence of otosclerotic foci at the site where it causes conductive hearing loss by interfering with the motion of the stapes or of the round window membrane **(3)**.

Otosclerotic plaques are mainly localized anterior to the oval window (fissula ante fenestram region), and on the stapes footplate (80%), at the round window (30%), pericochlear region (21%) and the anterior part of the internal auditory canal (19%). Other localizations although very rare have also been described: malleus, incus, facial canal, semicircular canals and endolymphatic duct **(4)**.

Treatment:

- **Non-surgical treatment:**
  - **Active monitoring (observation):**

In the early stages, the hearing loss might be significant enough to be felt by the patient, but audiological assessment might not justify surgical intervention (ABG < 30 dB). Additionally, some patients will choose not to have the surgery due to fear of its complications. In these cases, the patient is monitored with regular hearing assessments for deterioration of hearing. Surgery will be offered if hearing loss meets indication criteria, and the benefits of the procedure outweigh the risks **(2)**

  - **Conservative treatment:**

External hearing aids are offered to patients with small ABG and to those who do not wish or cannot have surgery. However, as hearing deteriorats, so will the effectiveness of these hearing aids. Patients who have almost no hearing or have lost their hearing completely can be considered for a cochlear implant **(2)**

- **Surgical treatment :**

The main therapeutical choice is stapes surgery. However, rarely alternative surgical approaches may be required such as bone anchored implantable devices, middle ear implants or cochlear implants, based on patient conditions and the severity of hearing loss **(2)**

Stapedotomy

- **Introduction:**

The patient should have a PTA demonstrating a conductive or mixed hearing loss (sometimes with a Carhart's notch) with a large enough ABG and absent stapedial reflexes. The affected ear should be the worse hearing ear. Speech discrimination should be sufficient to justify the risk of the procedure. Clinical examination should exclude other middle ear disease and the tympanic membrane should be intact. Imaging can help to confirm the clinical diagnosis or exclude other pathologies **(5)**.

- **The most common indications and contraindications (2):**
  - **Indication:**

Progressive conductive hearing loss.
Absent stapedial reflexes.
Air-bone gap greater than 20 dB in at least three frequencies.
Good speech discrimination.
Worse hearing ear.

  - **Contraindication:**

Perforated tympanic membrane.
Better hearing or only hearing ear.
Poor speech discrimination.
Air-bone gap less than 20 dB in at least three frequencies.
Ongoing middle ear disease.

Procedure (2):

- **Anaesthesia:**

The procedure can be done under general anaesthesia or local anaesthesia. The latter may be preferred as the patient can feedback to the surgeon what they are sensing such as improvement in hearing or dizziness. **(2)**

- **Tympanotomy:**

The middle ear is usually accessed via transcanal or endaural approach. When a transcanal approach is performed, an incision is done within the ear canal close to the tympanic membrane and the entire skin and membrane are lifted from the bone. When endaural approach is carried out, the skin incision is done in front of the root of the helix and continued into the posteriorsuperior part of the outer ear canal. Care must be taken when entering the middle ear so that the chorda tympani nerve, which supplies taste to the ipsilateral 2/3 of the tongue, is not injured. Also, care must be taken so as not to perforate tympanic membrane. **(2)**

- **Visualisation:**

The mains structures (stapes, its footplate, the oval window and the facial nerve) must be within the operating view. Lateral atticotomy (bone removal) is usually performed to achieve the required view with care taken not injure the chorda tympani nerve. **(3)**

- **Confirming fixation:**

Gently pushing of the ossicles to confirm fixation of the stapes. Fixation of the other ossicles due to another disease is rare but possible so their mobility must also be confirmed, otherwise the conductive hearing loss will persist. **(3)**

- **Removal of stapes superstructure:**

There are multiple steps in this part, but the aim is to remove the stapes bone without the footplate. Care is taken not to injure the facial nerve, which passes near the footplate as this can cause facial weakness on the operated side. Beneath the otic capsule, there is the membranous labyrinth containing the perilymph. Care must be taken so the membrane is not ruptured and for fluid not to leak out, as this can result in permanent hearing loss. **(3)**

- **Stapedotomy:**

A small holl (0.6-0.8 mm) is made through the posterior part of the footplate but taking care not to cause fracture. This step can be performed by laser, microdrill or manual perforator (pick).**(5)**

- **Prosthesis placement:**

Following the measurement of the distance between the long process of the incus and the stapedotomy hole, the correct size of prosthesis is chosen. One end of the prosthesis is placed into the stapedotomy hole and the other end is attached and crimped to the long process of the incus, bridging the gap between the incus and the vestibule. The mobility of the reconstructed ossicular chain is verified. **(5)**

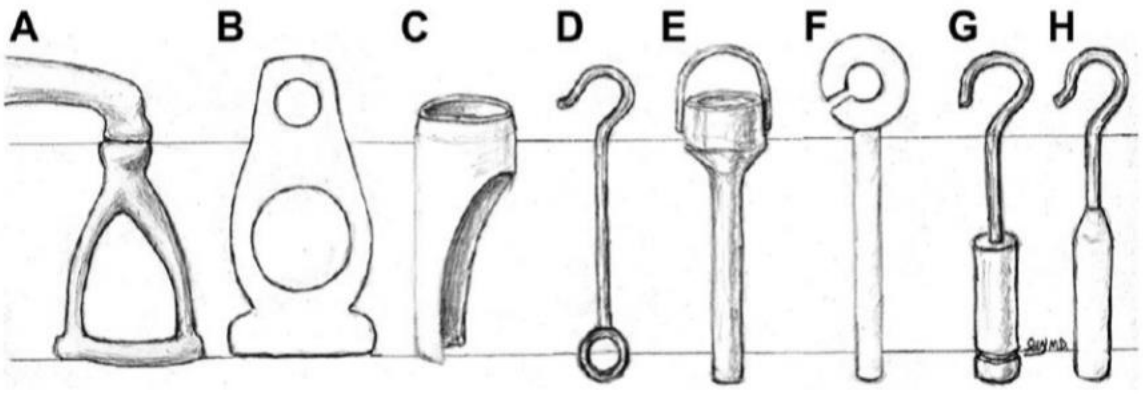

Figure 1: Different prosthesis over the years. Early and representative stapes prostheses. (A) Human stapes and incus long process; (B) first stapes prosthesis, Shea and Treace, carved Teflon fluoroplastic; (C) Shea strut, polyethylene; (D) House wire loop, stainless steel; (E) Robinson bucket handle, titanium; (F) fluoroplastic loop; (G) platinum wire hook, stainless steel piston; and (H) nitinol wire hook and fluoroplastic piston.**(6)**.

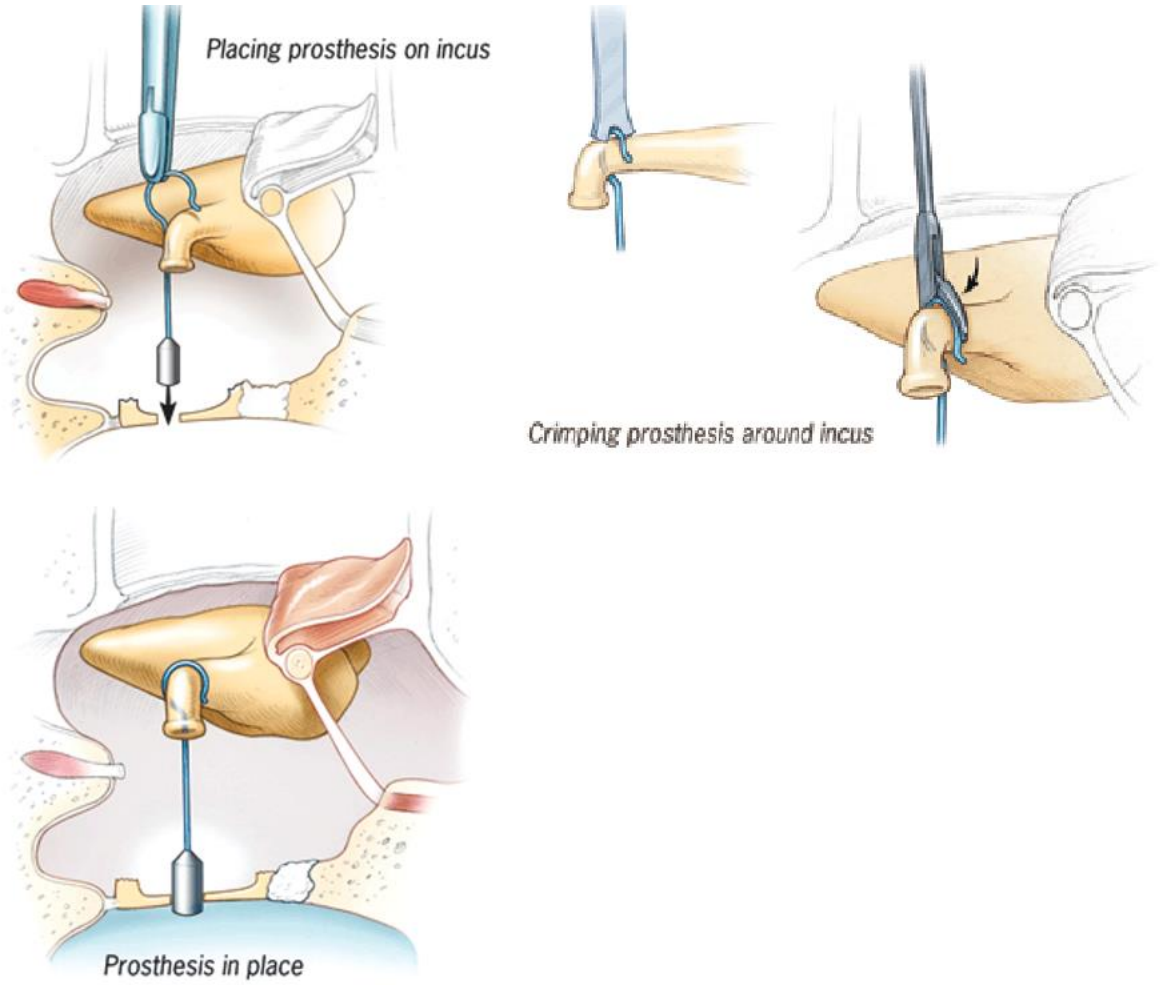

Figure 2: The basic steps of placing stapes prosthesis with crimping **(7)**.

- **sealing the hole of stapedotomy:**

Any space around the hole is filled with tissue. Various kinds of materials have been applied in the field of otology surgery to seal the oval window. These include perichondrium, adipose tissue, gelatin sponge (Gel foam), vein graft ,soft connective tissue, and blood clot **(8)** · **Faramarzi et al; (9)**recommend HAG as a safe sealing material after stapedotomy for otosclerosis.

- **Closure:**

The tympanic membrane and skin are placed back to their original positions and the incision is allowed to heal on its own with the transcanal approach. If the endaural approach was performed, the external incision needs to be sutured. If the tympanic membrane has been previously perforated, then closure with a fascia or cartilage graft is done at this stage. The ear canal is filled with antibacterial material to avoid wound infection. **(8)**

- **Follow-up:**

The patient is seen couple of weeks later to remove the antibacterial material and to assess the healing. They are seen once more about couple of months later, once healing is completed, to assess their hearing. Afterwards, they can have regular hearing assessments to ensure hearing is stable and for research purposes.

- **Possible complications (5):**

- **Dead ear:**

This term refers to a rare complication resulting in complete hearing loss and can occur due to perilymph leak, utricule injury, labyrinthitis or granuloma formation. Patient must be consulted about this possibility as they might choose to use hearing aids instead of undergoing surgery. **(5)**

- **Facial Weakness:**

The nerve runs through the middle ear and close to the oval window. A facial nerve monitor may be used to assist to find the path of the nerve and demonstrate normal functional just before closure. The weakness is almost always transient, as it is extremely rare for the facial nerve to be severed but the patient must be consulted about the possibility. **(5)**

- **Altered taste:**

The chorda tympani nerve is most of the time obstructing the operating view. Manipulation to marginalise the nerve is almost unavoidable during surgery. Like the facial weakness, the taste recovers in most cases except where the nerve was severed. This is more common than the facial nerve injury but still rare. **(8)**

- **Dizziness:**

Excessive movement of the inner ear fluid will affect the balance apparatus of the ear. This is mainly due to manipulation of the ossicles and the footplate which results in large amounts of kinetic energy to be transmitted to the vestibule. Again, this is usually transient. **(8)**

Tinnitus:

Ringing in the ear is common but recovery is certain. **(9)**

- **Pain:**

This is due to tissue damage, mainly the skin incision and bone removal to improve surgical view. The endoscopic approach requires smaller skin incision and rarely any bone removal. Thus, it should result in less pain. **(9)**

- **Tympanic membrane perforation:**

Tympanic membrane perforation is common in the community and surgical closure (myringoplasty) is greatly more common than stapes surgery. Thus, although unfortunate, this is a minor complication that can be fixed during the surgery. An extra scar might be present to harvest the necessary graft. **(9)**

Hyaluronic acid

Introduction:

HA is a natural glycosaminoglycan in the connective tissues, which is commonly used in tissue engineering **(10)**.

HA has been reported to be a useful material in the field of otology **(11)**.

With respect to the benefits of HA in otology, a few publications have revealed the potential effects of HA in sudden sensorineural hearing loss in terms of drug delivery to the cochlea **(12)**.

Moreover, several studies have confirmed the HA roles in myringoplasty **(13**). In the field of cochlear implant, preserved low-frequency hearing by injecting triamcinolone into cochleostomy site, which was then covered by a drop of HAG to seal the cochleostomy **(14)**.

There is a relatively small body of literature on the use of HAG in stapedotomy. In a basic study, **Angeli et al ;(15)** drilled the footplate through HAG with argon laser and then used fat as the sealing material. He found satisfactory results regarding postoperative hearing outcome, vertigo, and nystagmus .

HA Synthesis and Degradation:

Distinct further glycosaminoglycans that synthesized inside the cell in the Golgi apparatus and then secreted externally by exocytosis, HA is synthesized by three transmembrane enzymes - HA synthetase 1 (HAS1), HA synthetase 2 (HAS2), HA synthetase 3 (HAS3) **(16)**.

The turnover of the molecule is a quick process and its half-life fluctuates from 12–24 h in the skin to a few minutes in the bloodstream **(17)**.

The HA existing in the blood is catabolized in lymph nodes and in the liver, however that present in the tissues is degraded outside the cell by hyaluronidase, reactive oxygen species (ROS), superoxide, nitric oxide and peroxynitrite produced during inflamed or injured tissues, and inside the cell by the lysosomes **(18)**.

Mechanism of Action:

Some of its important biological properties are biocompatibility and natural degradation. As a viscoelastic cushion in the healing process, it has hydrophilic and lubricating properties. Also, this material has been shown to help proliferation of endothelial cells, cell adhesion, fibroblast proliferation and finally help wound healing **(10)**.

Medical Applications of HA and its Derivatives (22):

- **HA in Osteoarthritis and in Cartilage Regeneration:**

Different preparations of HA for OA treatment and cartilage regeneration are always being projected. **(10)**.

- **Ophthalmology:**

Topical agents into the eye drained quickly and HA combined with drugs might modulate the dose and the time of transport. This additional application of HA derivatives opens up further occasions for the study of medical and pharmaceutical applications of HA in ophthalmology. **(10)**.

- **Skin:**

The extensive field of uses of HA in skin healing processes appears obviously. HA and its derivatives have been tested either alone or combined with numerous other molecules to encourage wound healing by prompting proliferative, remodeling and angiogenetic processes. **(17)**.

- **Vascular Tissue:**

HA suggested for cell-based therapies, to generate vascularized tissue and motivate microvessels' formation for tissue ischemia therapy, nevertheless as a promoting factor for vascular graft endothelialization and as a vascular substitute. **(17)**.

- **Peripheral Nerve :**

HA can play a role in the therapy of peripheral nerve injury when applied in the form of hydrogel or in overtone either with natural molecules (collagen, chitosan) or with synthetic polymers (PLGA, Ply-L-Lysine) thus approving an extra surprising capacity of interacting with specific growth factors involved in peripheral nerve regeneration. **(18)**.

- **Adipose Tissue:**

HA experienced in many studies for adipose tissue engineering alone or combined with other bioactive material or drugs or cytokines, in order to avoid rapid resorption or even better to promote adipose tissue replacement. **(18)**.

- **Cancer Therapy:**

Only little therapeutics verified clinically and no HA-based drug delivery systems for human anticancer therapies are actually in clinical use. However, they clearly confirmed the potential for future use as cancer therapy. **(18)**.

- **Physical forms of hyaluronic acid (19):**

- **HA viscoelastic solutions:**

Viscoelastic solutions of HA do not keep long-lasting mechanical integrity. **(19)**

- **HA-Based scaffolds:**

Scaffolds are momentary auxiliary structures that can assistance in promoting cell and tissue ingrowth through biodegradable structures similar hydrogels. **(19)**

- **HA nanoparticles:**

Large molecule of HA cannot infiltrate the skin readily and maximum use of HA on skin occurs straight at the surface. Though, through the use of nanoparticles, HA can be transported deep into the skin and at high concentration without injection or physical skin penetration **(20)**.

United States Food and Drug Administration (FDA) Labeled Indications (21):

- **Intraarticular injection:**

For pain relief in patients with mild to moderate osteoarthritis (OA) of the knees, who have not responded to conservative non-pharmacological measures and/or analgesics. The FDA has not evaluated nor approved this treatment for any other joints. **(21)**

- **Intradermal injection:**

Injection into the mid-to-deep dermis for correction of facial wrinkles or folds and perioral rhytids. Patients must be over the age of 21. **(21)**

- **Subcutaneous injection:**

Volume deficit correction for dorsal hands in patients over the age of 21.
Correction of age-related volume loss and for cheek augmentation in mid-face in patients over the age of 21. **(21)**

- **Subperiosteal injection:**

Correction of age-related volume loss and for cheek augmentation in mid-face in patients over the age of 21. **(21)**

- **Submucosal injection:**

Injection into the lips for lip augmentation in patients over the age of 21.

- **Topical cream/gel:**

Management of wounds, skin ulcers.
Relief of symptoms (burning, itching, and pain) in dermatoses such as atopic dermatitis, radiodermatitis, and allergic contact dermatitis. **(21)**

- **Ophthalmic:**

Surgical aid cataract extraction, intraocular lens implantation, corneal transplant, glaucoma filtration, retinal attachment surgery, and anterior segment surgery.

- **Non-FDA-Labeled Indications (21):**

- Injection to provide a scaffold for regenerative endodontic procedures.
- Injection into vocal folds to treat glottal insufficiency.
- Injection into the areola to enhance nipple projection after breast reconstructive surgery.
- Refractory interstitial cystitis.
- sealing matterial in stapedotomy.

- **Contraindications (21):**

- Hypersensitivity to hyaluronic acid or any of the formulation components.
- History of severe allergic reaction or anaphylaxis to hyaluronic acid.
- Hypersensitivity reaction to gram-positive bacterial proteins (for products derived from bacterial source).
- Hypersensitivity reaction to lidocaine (for products containing lidocaine).
- Bleeding disorder.

The safety and efficacy of hyaluronic acid injections in pregnant females, lactating females, and the pediatric population have not been established. **(21)**

References:

1. Clarke-Brodber, A. L., & Taxy, J. B. (2021). The stapes in otosclerosis: Osteoarthritis of an ear ossicle. Head and Neck Pathology, 1-6.
2. Quesnel, A. M., Ishai, R., & McKenna, M. J. (2018). Otosclerosis: temporal bone pathology. Otolaryngologic Clinics of North America, 51(2), 291-303.
3. Foster, M. F., & Backous, D. D. (2018). Clinical Evaluation of the Patient with Otosclerosis. Otolaryngologic Clinics of North America, 51(2), 319-326.
4. Yagi, C., Morita, Y., Takahashi, K., et al. (2019). Otosclerosis: anatomical distribution of otosclerotic loci analyzed by highresolution computed tomography. European Archives of OtoRhino-Laryngology, 276(5), 1335-1340

5. Alexandros, K. (2023). Innovations in stapes surgery.
6. Sevy, A., & Arriaga, M. (2018). The stapes prosthesis: past, present, and future. Otolaryngologic Clinics of North America, 51(2), 393-404.
7. White, T. (2022). Draw together: Artist and surgeons convey the body's secrets.
8. Liu YF, Gupta A, Nguyen SA, Lambert PR, Jung TT (2020) Preferences in stapes surgery among American otological society otologists. World J Otorhinolaryngol Head Neck Surg 6(1):59–65.
9. Faramarzi M, Roosta S, Aminpour S.(2019) Comparing Gelfoam vs fat as a sealing material in stapedotomy: A prospective double-blind randomized clinical trial. Clin Otolaryngol, 44:299–304.
10. He Y, Hou Z, Wang J, Wang Z, Li X, Liu J, XiaolinYang LQ, Zhao J (2020) Assessment of biological properties of recombinant collagen-hyaluronic acid composite scafolds. Int J Biol Macromol 149:1275–1284.
11. Daou, C. A. Z., & Bassim, M. (2020). Hyaluronic acid in otology: Its uses, advantages and drawbacks-A review. American Journal of Otolaryngology, 41(2), 102375.
12. Rogha, M., and Kalkoo, A. (2017). Therapeutic Effect of Intra-tympanic Dexamethasone–Hyaluronic Acid Combination in Sudden Sensorineural Hearing Loss. Iran. J. Otorhinolaryngol. 29 (94), 255–260.
13. Fouad, Y. A., Abdelhady, M., El-Anwar, M., & Merwad, E. (2018). Topical platelet rich plasma versus hyaluronic acid during fat graft myringoplasty. American Journal of Otolaryngology, 39(6), 741-745.
14. Kiefer J, Gstoettner W, Baumgartner W, Pok SM, Tillein J, Ye Q, von Ilberg C (2004) Conservation of low-frequency hearing in cochlear implantation. Acta Otolaryngol 124(3):272–280.
15. Angeli SI (2006) Hyaluronate gel stapedotomy. Otolaryngol Head Neck Surg 134(2):225–231.
16. Itano, N., & Kimata, K. (2002). Mammalian hyaluronan synthases. IUBMB life, 54(4), 195-199.
17. Fraser, J. R. E., Laurent, T. C., & Laurent, U. B. G. (1997). Hyaluronan: its nature, distribution, functions and turnover. Journal of internal medicine, 242(1), 27-33.
18. Heldin, P., Lin, C. Y., Kolliopoulos, C., Chen, Y. H., & Skandalis, S. S. (2019). Regulation of hyaluronan biosynthesis and clinical impact of excessive hyaluronan production. Matrix Biology, 78, 100-117.
19. Dovedytis, M., Liu, Z. J., & Bartlett, S. (2020). Hyaluronic acid and its biomedical applications: A review. Engineered Regeneration, 1, 102-113.
20. Brown, M. B., & Jones, S. A. (2005). Hyaluronic acid: a unique topical vehicle for the localized delivery of drugs to the skin. Journal of the European Academy of Dermatology and Venereology, 19(3), 308-318.
21. Walker, K., Basehore, B. M., Goyal, A., & Zito, P. M. (2018). Hyaluronic acid.
22. Abatangelo, G., Vindigni, V., Avruscio, G., Pandis, L., & Brun, P. (2020). Hyaluronic acid: redefining its role. Cells, 9(7), 1743.