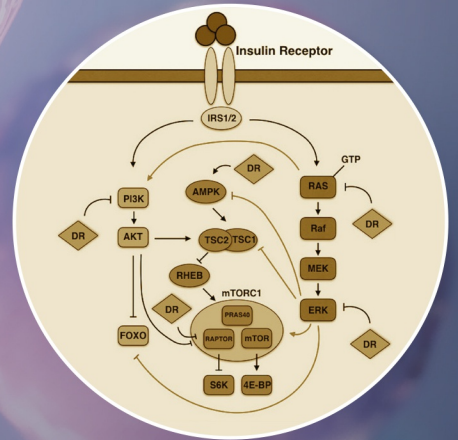
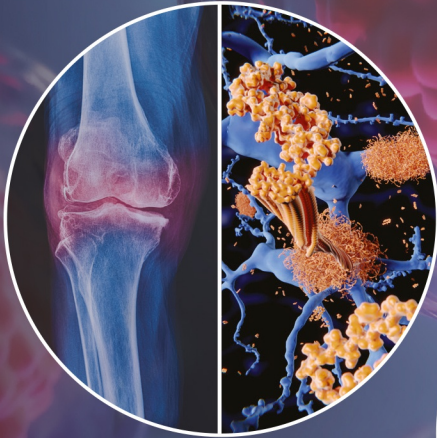


BEAUTY, AGING, AND ANTIAGING



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BEAUTY, AGING, AND ANTIAGING

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15. Dental-periodontal structures and aging

BUKET ACAR AND ABDULLAH C. AKMAN

- Aging and oral health 143
- Inflammaging and oral tissues 144
- Tooth loss and edentulism in the elderly population 145
- Physiological and pathological changes of the oral tissues due to aging 147
- Regenerative periodontal treatment in the elderly 147
- Pulp regeneration in elderly 148
- Regenerative therapies for xerostomia 149
- Conclusions 149
- References 149

II

Regenerative and restorative medicine

16. Antiaging: Is it possible?

ARDA KUCUKGUVEN AND İBRAHİM VARGEL

- Introduction 155
- Alternative approaches to aging 155
- Senolytics 156
- Senostatics 157
- Conclusions 158
- References 159

17. Antiaging principles in plastic surgery

ARDA KUCUKGUVEN AND İBRAHİM VARGEL

- Introduction 161
- Effects of aging on tissues 161
- Can plastic surgery prevent aging? 162
- Surgical treatment of age-related changes in plastic surgery 164
- References 170

18. Regenerative cell therapy for antiaging

ERAY COPCU AND SULE ÖZTAN

- Regenerative medicine and aging 173
- Stromal/stem cell 173
- Stromal-cell isolation techniques 176

- Neither nanofat nor SVF: TOST 180
- PRP/PPP/TOST and combination: Enhanced regeneration 185
- Adjustable regenerative adipose-tissue transfer (ARAT) 185
- Further reading 194

19. Energy based procedures in facial cosmetic and rejuvenation

HUSEYİN GÜNER, CAGIL MERIC ERENOĞLU, AND BILGEN KATIPOĞLU ERENOĞLU

- Lasers 198
- Intense pulsed light (IPL) 200
- Focused ultrasound 201
- Radiofrequency (RF) 201
- References 202

20. How to induce antiaging in plastic surgery

ZEKERİYA TOSUN AND FATMA ÖZ BAĞCI

- Lipofilling 205
- Conclusion 209
- Acknowledgment 209
- References 209

21. Minimally invasive treatments for the aging face

HALİL İBRAHİM CANTER AND MAJİD İSMAYİLZADA

- Aging process in general 211
- Wrinkles 212
- Sagging 214
- Volume loss 216
- Skin quality 217
- Points to consider 218
- References 219

22. Cosmetic surgical treatments for the aging face

OZAN BITİK

- Age heterogeneity 223
- Objectives 224
- Basic principles 224
- Surgical techniques 224
- Conclusion 232
- References 235

Antiaging principles in plastic surgery

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Introduction

Staying young and preventing the effects of aging are common goals in many different cultures. Currently, we are not able to stop aging and stay young forever, but we have made significant progress in revealing the senescence mechanisms and development of invasive techniques, biotechnology, and pharmaceuticals to reverse or delay aging-related changes up to a point. The aging process and its effects occur gradually at the cellular and tissue levels, including skin, ligaments, muscles, and bone.

It is important to understand that tissues are affected at different rates during aging, which is apparent externally when we look at someone's face. Different tissues respond to aging differently, for example, bone resorption occurs during aging, whereas skin loses elasticity and begins to sag. In this chapter, we explain the aging-related changes associated with plastic surgery briefly and highlight which antiaging principles are used to reverse or treat these effects.

Effects of aging on tissues

Skin

Aging skin undergoes epidermal thinning and atrophy. Its cellular turnover becomes slower.¹⁻³ However, it continues to have a strong barrier function throughout life regardless of aging-related changes.^{3,4} As the dermis ages, it becomes thinner and undergoes atrophy. Its cellular turnover, extracellular matrix, and vascularity decrease.^{1,3,5} During aging, collagen fibril orientation of the dermis becomes disorganized, and the fibrils reduce in size and number and fragment.¹⁻⁴ The amount of dermal collagen also reduces, which is caused by decreased collagen production due to aged fibroblasts and increased function of metalloproteinases.^{2,4}

There are several alterations in wound-healing mechanisms with aging.^{6,7} The wound-healing process becomes slower with aging but is not defective if the individual is healthy.⁸ However, if comorbidities are added to age-related skin- and wound-healing alterations, this might

lead to development of chronic wounds.⁸ Approximately 10% of hospitalized elderly patients develops nonhealing pressure ulcers.^{9,10} Despite adverse effects of aging on wound healing, scar quality of healthy elderly individuals is high due to their accelerated wound maturation compared with younger patients.¹¹

It is well known that regardless of age, skin still has regenerative functions, which can be proved by clinical outcomes of skin rejuvenation treatments such as chemical peels, retinoic acid, microneedling, and laser resurfacing.^{12,13} Plastic surgeons, dermatologists, and the cosmetic industry have common interest in nonsurgical skin-rejuvenation procedures.¹⁴ These procedures can also be combined with more invasive treatments to treat age-related skin alterations.^{15,16}

Adipose tissue

Proinflammatory cytokines are released from adipose tissue with aging, which deteriorates regeneration by inhibiting preadipocyte differentiation.^{17,18} Adipocytes are reduced in size, and how they react to insulin changes due to these cytokines, which also stimulate lipolysis.¹⁷ Subcutaneous fat is also affected by senescence.¹⁹ Redistribution of fat toward ectopic and visceral localizations occurs with aging. Deposition of fat leads to local effects contributing to systemic dysfunction and lipotoxicity.^{2,17,18,20} It is crucial to understand the changes of adipose tissue with aging since it is gaining importance as a great source for volume restoration and rejuvenation procedures with its high stem cell content.

Muscle

Human muscle mass decreases up to 30% by 80 years of age.²¹ Its function and strength also decline during senescence.^{21,22} Skeletal muscle atrophy (sarcopenia) or catabolism are seen because of the increased number of inflammatory cytokines and decreased muscle anabolism. Limitation of regenerative function of satellite cells and stem cells compromises the reparative

function in aged muscles. Accumulation of fat, increased fibrosis, and decreased volume and capacity of restoration cause muscle atrophy and functional loss.^{21–23}

Bone

Bone tissue undergoes resorption and volume loss during aging.²⁴ Its mineral content including phosphate and calcium stores decreases, and bone marrow fat content increases with aging.²⁵ Osteoclasts, osteoblasts, progenitor cells, and osteocytes have altered function leading to decrease in skeletal strength and osteoporosis, which increases the risk of fractures.^{20,26}

Mendelson and Wong showed that the pyriform region of the nose, the inferolateral and superomedial parts of the orbital rim, and the prejowl region of the mandible undergo resorption with aging.²⁴ The areas of resorption are highly predictable, which has a strong clinical relevance in facial rejuvenation. Therefore, clinicians should be aware of these alterations to implement proper noninvasive and invasive procedures in aging patients.

Nerve

Several physiological and anatomical changes are seen in aged nerves. Schwann cells' regenerative capacity decreases significantly due to deterioration of their repair response in face of injury.²⁷ Aging-related changes result in decline in sensory perception, autonomic responses, nerve conduction velocity, and muscle strength.^{28–30} Therefore, capability of reinnervation and regeneration following nerve injuries is compromised and becomes less effective during senescence.³¹

Can plastic surgery prevent aging?

We can basically divide the principals of management of aging-related changes in plastic surgery into two categories: regenerative and restorative treatments. Restorative treatments are considered more invasive procedures

aiming to correct what is affected due to aging. Regenerative procedures, on the other hand, focus on providing optimal parameters including microenvironment, growth factors, and so on for tissue regeneration. In regenerative procedures, the main subject is the tissue itself, whereas in rejuvenation processes the necessary factors are organized and optimal conditions are provided to facilitate or initiate rejuvenation. With the current knowledge on plastic surgery, we can conclude that we cannot prevent but only delay aging by providing optimal factors for tissue regeneration and by removing external deleterious factors.

Rejuvenation

Topical

Aging-related skin alterations can be addressed by noninvasive topical treatments. Prevention is key in reducing the impact of aging on tissues similar to other areas of medicine. Photoprotection and reduction of UV exposure by barriers including sunscreens, UV-protective clothing, and hats minimize extrinsic skin changes. Chemical sunscreens (organic sunscreens) transform UV irradiation into heat, which is dissipated from the epidermis. Physical sunscreens (inorganic sunscreens) have titanium dioxide and zinc oxide particles, which reflect light rather than absorbing it.³² Several topical antioxidants (e.g., vitamin C) neutralize extracellular and intracellular free radicals and prevent the deleterious effects of UV light. They can also induce neocollagenesis.³³

Vitamin A derivatives (retinoids) are also very strong and popular compounds in the treatment of age-related skin alterations and photodamage. They provide significant improvement in the skin by functioning at the molecular level. They promote gene expression, induce fibroblast proliferation and neocollagenesis, and inhibit matrix metalloproteinases. Regular use of retinoids provides smoother skin by eliminating or decreasing coarse and fine rhytids and

correcting irregular pigmentation. These effects result in a more harmonious and balanced skin with homogeneous texture.³⁴

Increasing skin exfoliation is another effective method to treat rhytids and hyperpigmentation. Alpha hydroxyl acids (e.g., lactic acid, glycolic acid), trichloroacetic acid, and phenol-croton oil are frequently used in plastic surgery to increase cellular turnover by increasing skin exfoliation. These chemical peels are easy to use and have significant effects on rhytids. Particularly, croton oil peeling is a very effective procedure in the management of deep perioral rhytids. It is also possible to increase their strength by altering their density, but this might increase the rate of adverse effects and should be executed by experienced physicians only.³³

Recently, peptides and growth factors have gained popularity in rejuvenation treatments. They essentially induce collagen synthesis at the molecular level, however, there is still little evidence to prove their efficacy in the treatment of aging-related skin or subcutaneous tissue changes.^{32,33}

Energy based

Skin quality can be improved with ablative and nonablative laser treatments. They can be used alone or in conjunction with other treatments including topical compounds, fillers, and surgery. Their versatile applications in plastic surgery make them an essential tool in the field of antiaging. Treatment of skin laxity, rhytids, pigmentation, and vascular lesions can be performed with laser-based devices. The type of treatment, patient's skin type, and level of tolerance are important parameters in deciding the type of laser that is going to be used. Ablative or nonablative, and fractional or nonfractional lasers, can be used according to patient needs.

The least invasive type is the 640-nm nonablative and nonfractional laser, which is the most tolerated type of energy-based treatment used for stimulation of collagen synthesis and elimination of fine rhytids. Its less-invasive nature causes minimal discomfort and downtime,

whereas multiple sessions are needed to reach a satisfactory outcome. Fractional and nonablative lasers are used for more complicated cases. They cause fractional thermolysis, which induces collagen synthesis and treats dyschromia. Skin tightening is a good indication for these lasers, but multiple sessions are also required. Ablative lasers are reserved for the most severe cases. They cause thermal necrosis and long downtime. However, they are very effective for deep rhytids and provide better improvement in skin tone, quality, and pores.³⁵

Radiofrequency devices are another energy-based technology for antiaging treatments. They are used for skin rejuvenation and function through electromagnetic energy to stimulate dermal collagen remodeling by thermal energy. Additionally, intense focused ultrasound produces acoustic energy that transforms into heat in the tissues, causing coagulation necrosis.^{36,37} These two energy-based devices have modest effects on skin rejuvenation.

Injectables

Neurotoxins

Botulinum toxin A injections to treat dynamic or static rhytids are common for reversing or delaying aging-related changes on the skin. This paralyzing agent helps to eliminate wrinkles and elevate eyebrows, thereby blocking neuromuscular junctions. The most common area of injection is the upper third of the face. Typically, its clinical effects start 2–3 days after injection and reach the maximal level at the end of 2 weeks. Its effects last approximately 4 months. The frontalis muscle, procerus muscle, and orbicularis oculi muscles are addressed to give a fresh look to patients, thereby eliminating horizontal and vertical lines of the forehead and treating crow's feet. The depressor anguli oris muscle is another potential target in patients with Marionette lines. It is also possible to treat visible platysmal bands by neurotoxin injections. Additionally, perioral wrinkles apparent with aging can be addressed by orbicularis oris injections.³⁸

It is very important to adjust and decide on the precise units needed for each injection point, which necessitates a combination of knowledge and experience. Even in experienced hands, several adverse effects or complications can be seen such as eyelid ptosis, swallowing difficulty, oral incompetence, and so on.³⁸

Soft tissue fillers

Aging-related volume loss and skin laxity correction with soft tissue fillers are increasingly popular (Fig. 1). Hyaluronic acid is the most popular filler used to address these changes. Calcium hydroxyapatite and poly-L-lactic acid are other popular fillers used for restoration of the aging face. These contents have different longevity in tissues due to their different viscosity, elasticity, and biodegradation properties.

Bone and fat resorption with aging can be restored with fillers, which additionally elevates the skin. For example, malar augmentation affects nasolabial folds and prejowl region by elevating the skin upwards (Fig. 2). Facial fat atrophy caused by aging or HIV infection can also be addressed with fillers as well as autologous fat grafting. Temple and malar region are common areas of facial fat atrophy. Additionally, same principles can also be used for aging hands. Dorsal subcutaneous fat tissue undergoes atrophy with aging, which can be restored with soft tissue fillers or fat grafting.

Surgical treatment of age-related changes in plastic surgery

Upper face

It is vital to understand aging-related changes and their underlying mechanisms to treat or prevent them. Forehead rhytids become apparent with the activity of mimic muscles including frontalis, corrugator, and procerus muscles. Volume loss and decrease in skin quality also contribute to these changes. Brow ptosis, excessive eyelid skin, involuntional eyelid ptosis, and lower eyelid laxity are examples of aging-related changes in

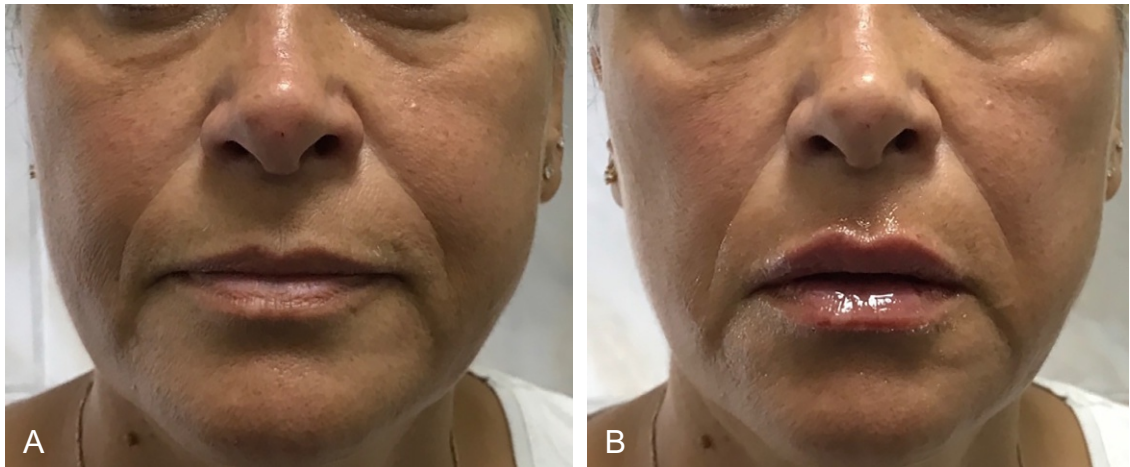


FIG. 1 Aging lip loses volume. Fillers can be used to restore volume deficiency. A 62-year-old woman has signs of aging in the perioral region. Nasolabial lines, Marionette lines, and volume loss of the lips can be seen.



FIG. 2 Hyaluronic acid fillers were used in a 59-year-old woman. Lips (total, 1 cc), mentum (total, 1 cc), mandibular border (unilateral, 2 cc), and malar region (unilateral, 1.5 cc) were treated with soft tissue fillers to restore volume loss and soft tissue descent.

the upper face. It is crucial to implement the right surgical technique to address these changes. For each problem, many techniques have been described. Morbidity, longevity, and technical difficulties differ greatly according to the technique.³⁹

Forehead horizontal lines can be eliminated with forehead lift, thereby addressing the frontalis muscle. Endoscopic technique, subcutaneous, or direct browlift techniques can be performed for brow ptosis, which helps reduce the amount of skin necessary to be removed in upper blepharoplasty (Fig. 3). Involuntary eyelid ptosis can be corrected with levator

advancement technique (Fig. 4). Herniated upper and lower orbital fat pads can be addressed during upper and lower blepharoplasty procedures, respectively (Fig. 5). Excess lower eyelid skin caused by aging can be removed with pinch blepharoplasty or conventional lower eyelid blepharoplasty with a subciliary approach. Lower eyelid laxity can be seen with aging due to lateral canthal tendinous loosening. This might result in ectropion or xerophthalmia. Canthoplasty, canthopexy, or lateral tarsal strip techniques are effective procedures to correct these problems.



FIG. 3 A subcutaneous browlift surgery, pinch lower blepharoplasty, and cantopexy were performed in a 47-year-old woman with brow ptosis and skin excess in the lower eyelid. Note the browlift surgery eliminated the need for upper blepharoplasty. Periocular rejuvenation is key to achieve pleasing outcomes in antiaging treatments in plastic surgery.

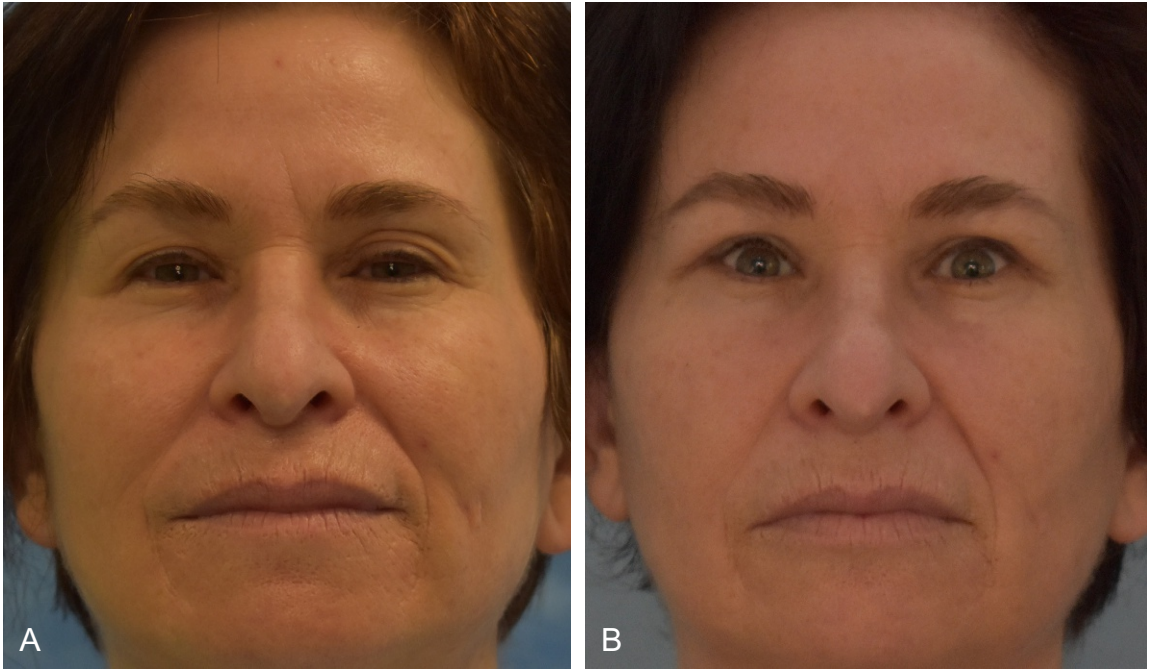


FIG. 4 Involutional eyelid ptosis is common in aging women. Levator aponeurosis detaches from the tarsal plate with aging. This 59-year-old woman underwent bilateral levator advancement surgery.



FIG. 5 Lower blepharoplasty is indicated when patients have under-eye bags and excess lower eyelid skin. This 45-year-old man underwent a lower blepharoplasty with a subciliary approach. The herniated fat pads and excess skin were removed.

Midface

Malar volume loss and descent are hallmarks of the aging midface. Volumization of the malar region with fat grafting, midface lift, or facelift procedures can be performed to correct malar soft tissue descent and bone resorption. Endoscopic techniques, midface lift with a subciliary approach, or facelift surgery are common ways to address these aging-related changes.

It is important to emphasize that fat grafting is a great adjunct with its high rejuvenation potential due to its rich stem cell content. Fat grafting can be used for both volumization with variable resorption rates and rejuvenation in any body region to correct aging-related alterations.⁴⁰

Lower face and neck

Perioral rhytids, Marionette lines, jowling, loss of mandibular sharpness due to soft tissue and submandibular gland descent, and increase of cervicomenal angle due to fat accumulation and platysmal laxity are common signs of the aging lower face (Fig. 6). There are many minimally invasive and invasive treatment options to correct these various changes. Neck lift with a submental approach allows supraplatysmal and subplatysmal fat reduction and platysmal tightening maneuvers to give a better contour to neck. Submandibular glands can also be excised in this approach if needed. Thread lift is becoming popular owing to its minimal morbidity and ease of application. However, it has a temporary effect and therefore should not be considered as a substitute for facelift and neck lift procedures. Facelift surgery allows manipulation of the SMAS and facial fat compartments, which results in a more defined mandibular contour and malar prominence.

Lips lose volume and upper lip skin becomes longer with aging. Volumization of lips with fillers or fat grafting, and procedures including lip lifting, can give a youthful appearance to the perioral region.⁴¹

Breast

Breastfeeding and gravity affect the shape of the breast. Breasts look deflated and flaccid with aging. Two parameters should be considered to give a more youthful appearance to the breast: breast volume and descent (Fig. 7). Autologous fat grafting or breast implants are common ways to restore volume, but are not always sufficient to achieve a pleasing outcome. Mastopexy is a procedure that lifts the nipple-areola complex along with a certain amount of breast tissue removal depending on the patient's breast anatomy. Breast content changes with aging and breastfeeding. It is not always possible to return to the original anatomy due to decreased skin elasticity. Therefore, each patient should be evaluated carefully, and customized interventions should be designed based on their expectations and anatomy.

Aging is a major risk factor for breast cancer. Majority of breast cancers are diagnosed in women older than 65 years.⁴² After oncologic surgery, breast reconstruction is an important procedure to restore the self-esteem of the individual. This can be performed by plastic surgeons using autologous and/or implant-based techniques.

Others

Pressure ulcers are very common in hospitalized elderly patients and should be managed either conservatively or with surgical procedures depending on the ulcer grade and patient's comorbidities.⁴³ Aging-related comorbidities such as diabetes can cause diabetic foot, which can be treated with plastic surgery principles including grafts or flaps, if the patient's disease is under control. Aging is also a predictive factor for several skin cancer types such as basal cell carcinoma, squamous cell carcinoma, and malignant melanoma.⁴⁴ All these tumors have different treatment principles in plastic surgery, ranging from simple excisional biopsy



FIG. 6 A 53-year-old woman with signs of facial aging underwent browlift, cantopexy, facelift, neck lift, and fat grafting. Rejuvenation of the face with a more youthful appearance was achieved.

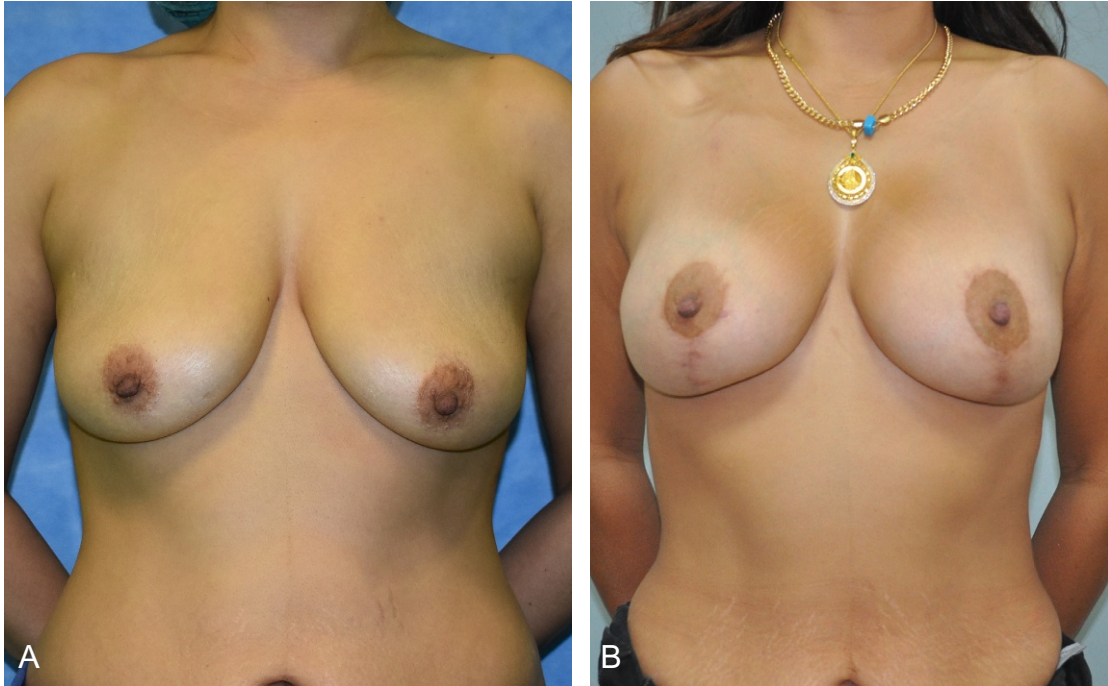


FIG. 7 A 33-year-old women with a history of two pregnancies underwent an augmentation mastopexy with implants. Note the breast ptosis in the preoperative photos.

to extremity amputation or lymph node dissection. All these aging-related changes and diseases might be delayed and alleviated with the help of antiaging treatments in the future. It is our mission to have a comprehensive knowledge about aging-related changes and mechanisms related to our profession and modify our approach to patients based on these developments as we witness the rise of preventive medicine.

References

1. Khavkin J, Ellis DA. Aging skin: histology, physiology, and pathology. *Facial Plast Surg Clin North Am* 2011;**19**(2):229–34.
2. Rittie L, Fisher GJ. Natural and sun-induced aging of human skin. *Cold Spring Harb Perspect Med* 2015;**5**(1), a015370.
3. Farage MA, Miller KW, Elsner P, Maibach HI. Structural characteristics of the aging skin: a review. *Cutan Ocul Toxicol* 2007;**26**(4):343–57.
4. Kohl E, Steinbauer J, Landthaler M, Szeimies RM. Skin ageing. *J Eur Acad Dermatol Venereol* 2011;**25**(8):873–84.
5. Callaghan TM, Wilhelm KP. A review of ageing and an examination of clinical methods in the assessment of ageing skin. Part I: cellular and molecular perspectives of skin ageing. *Int J Cosmet Sci* 2008;**30**(5):313–22.
6. Gosain A, DiPietro LA. Aging and wound healing. *World J Surg* 2004;**28**(3):321–6.
7. Sgonc R, Gruber J. Age-related aspects of cutaneous wound healing: a mini-review. *Gerontology* 2013;**59**(2):159–64.
8. Gould L, Abadir P, Brem H, et al. Chronic wound repair and healing in older adults: current status and future research. *J Am Geriatr Soc* 2015;**63**(3):427–38.
9. Maklebust J, Magnan MA. Risk factors associated with having a pressure ulcer: a secondary data analysis. *Adv Wound Care* 1994;**7**(6):25. 27–28, 31–24 passim.

10. Margolis DJ, Bilker W, Knauss J, Baumgarten M, Strom BL. The incidence and prevalence of pressure ulcers among elderly patients in general medical practice. *Ann Epidemiol* 2002;**12**(5):321–5.
11. Bond JS, Duncan JAL, Sattar A, et al. Maturation of the human scar: an observational study. *Plast Reconstr Surg* 2008;**121**(5):1650–8.
12. Carniol PJ, Hamilton MM, Carniol ET. Current status of fractional laser resurfacing. *JAMA Facial Plast Surg* 2015;**17**(5):360–6.
13. Ramaut L, Hoeksema H, Pirayesh A, Stillaert F, Monstrey S. Microneedling: where do we stand now? A systematic review of the literature. *J Plast Reconstr Aesthet Surg* 2018;**71**(1):1–14.
14. Lee CM. Fifty years of research and development of cosmeceuticals: a contemporary review. *J Cosmet Dermatol* 2016;**15**(4):527–39.
15. Koch BB, Perkins SW. Simultaneous rhytidectomy and full-face carbon dioxide laser resurfacing: a case series and meta-analysis. *Arch Facial Plast Surg* 2002;**4**(4):227–33.
16. Fulton JE. Simultaneous face lifting and skin resurfacing. *Plast Reconstr Surg* 1998;**102**(7):2480–9.
17. Pararasa C, Bailey CJ, Griffiths HR. Ageing, adipose tissue, fatty acids and inflammation. *Biogerontology* 2015;**16**(2):235–48.
18. Zamboni M, Rossi AP, Fantin F, et al. Adipose tissue, diet and aging. *Mech Ageing Dev* 2014;**136–137**:129–37.
19. Palmer AK, Kirkland JL. Aging and adipose tissue: potential interventions for diabetes and regenerative medicine. *Exp Gerontol* 2016;**86**:97–105.
20. Farr JN, Fraser DG, Wang H, et al. Identification of senescent cells in the bone microenvironment. *J Bone Miner Res* 2016;**31**(11):1920–9.
21. Ali S, Garcia JM. Sarcopenia, cachexia and aging: diagnosis, mechanisms and therapeutic options—a mini-review. *Gerontology* 2014;**60**(4):294–305.
22. Lang T, Streeper T, Cawthon P, Baldwin K, Taaffe DR, Harris TB. Sarcopenia: etiology, clinical consequences, intervention, and assessment. *Osteoporos Int* 2010;**21**(4):543–59.
23. Sousa-Victor P, Garcia-Prat L, Serrano AL, Perdiguero E, Munoz-Canoves P. Muscle stem cell aging: regulation and rejuvenation. *Trends Endocrinol Metab* 2015;**26**(6):287–96.
24. Mendelson B, Wong CH. Changes in the facial skeleton with aging: implications and clinical applications in facial rejuvenation. *Aesthetic Plast Surg* 2020;**44**(4):1151–8.
25. Boros K, Freemont T. Physiology of ageing of the musculoskeletal system. *Best Pract Res Clin Rheumatol* 2017;**31**(2):203–17.
26. Ensrud KE. Epidemiology of fracture risk with advancing age. *J Gerontol A Biol Sci Med Sci* 2013;**68**(10):1236–42.
27. Painter MW, Brosius Lutz A, Cheng YC, et al. Diminished Schwann cell repair responses underlie age-associated impaired axonal regeneration. *Neuron* 2014;**83**(2):331–43.
28. Verdu E, Ceballos D, Vilches JJ, Navarro X. Influence of aging on peripheral nerve function and regeneration. *J Peripher Nerv Syst* 2000;**5**(4):191–208.
29. Pannese E. Morphological changes in nerve cells during normal aging. *Brain Struct Funct* 2011;**216**(2):85–9.
30. Drac H, Babiuch M, Wisniewska W. Morphological and biochemical changes in peripheral nerves with aging. *Neuropatol Pol* 1991;**29**(1–2):49–67.
31. Kovacic U, Sketelj J, Bajrovic FF. Chapter 26: Age-related differences in the reinnervation after peripheral nerve injury. *Int Rev Neurobiol* 2009;**87**:465–82.
32. Clark A, Hessler JL. Skin care. *Facial Plast Surg Clin North Am* 2015;**23**(3):285–95.
33. Thomas JR, Dixon TK, Bhattacharyya TK. Effects of topicals on the aging skin process. *Facial Plast Surg Clin North Am* 2013;**21**(1):55–60.
34. Hubbard BA, Unger JG, Rohrich RJ. Reversal of skin aging with topical retinoids. *Plast Reconstr Surg* 2014;**133**(4):481e–90e.
35. Mirza HN, Mirza FN, Khatri KA. Outcomes and adverse effects of ablative vs nonablative lasers for skin resurfacing: a systematic review of 1093 patients. *Dermatol Ther* 2021;**34**(1), e14432.
36. Greene RM, Green JB. Skin tightening technologies. *Facial Plast Surg* 2014;**30**(1):62–7.
37. Rostan EF. Combining laser therapies for optimal outcomes in treating the aging face and acne scars. *Facial Plast Surg Clin North Am* 2012;**20**(2):221–9. vii.
38. Janes LE, Connor LM, Moradi A, Alghoul M. Current use of cosmetic toxins to improve facial aesthetics. *Plast Reconstr Surg* 2021;**147**(4):644e–57e.
39. Gerth DJ. Structural and volumetric changes in the aging face. *Facial Plast Surg* 2015;**31**(1):3–9.
40. Tonnard P, Verpaele A, Carvas M. Fat grafting for facial rejuvenation with nanofat grafts. *Clin Plast Surg* 2020;**47**(1):53–62.
41. Wollina U. Perioral rejuvenation: restoration of attractiveness in aging females by minimally invasive procedures. *Clin Interv Aging* 2013;**8**:1149–55.
42. Lichtman SM, Hurria A, Jacobsen PB. Geriatric oncology: an overview. *J Clin Oncol* 2014;**32**(24):2521–2.
43. Fremmelevholm A, Soegaard K. Pressure ulcer prevention in hospitals: a successful nurse-led clinical quality improvement intervention. *Br J Nurs* 2019;**28**(6):S6–S11.
44. Gordon R. Skin cancer: an overview of epidemiology and risk factors. *Semin Oncol Nurs* 2013;**29**(3):160–9.