Nonsurgical aesthetic procedures

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List of Abbreviations:

BTX - botulinum toxin

BTX-A - botulinum toxin type A

BTX-B - botulinum toxin type B

HA- hyaluronic acid

CaHA - calcium hydroxylapatite

PMMA microspheres - Polymethylmethacrylate microspheres

AHAs - alpha-hydroxy acids

TCA - trichloroacetic acid

FDA – Food and Drug Administration

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2 Summary

Title: Nonsurgical aesthetic procedures

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Summary:

Everyone's desire is to become the best version of the themselves, especially when it comes to the appearances and that has driven the development of various aesthetic procedures. Especially non-surgical procedures are lately gaining much of attention, as they represent less risk and are also more affordable for the patient.

This article provides an overview of the most common nonsurgical aesthetic procedures currently in use together with reasons for their growing popularity. We will start with the background of how it all started and advanced and look closer at the process of aging, in order to understand the changes which are later addressed through the treatments. Most common complications that may occur will be mentioned. The review will also look into the pain management techniques most commonly offered to the patient in order to make the treatment more pleasant experience. Finally, this article will discuss the importance of checking the patient's smoking status pre-procedurally, the different approach that should be taken when dealing with male patient and have an insight into ethical aspect.

In order to select the best approach for individual patient we must consider many factors, such as their health conditions, unique anatomic characteristics, tissue quality as well as take into account their expectations. This way we will also achieve the best results.

Keywords: nonsurgical aesthetic procedures, botulinum toxin (BTX), dermal fillers, deoxycholic acid, chemical peels, microneedling, lasers, nonsurgical rhinoplasty, pain management, smoking, male patients, ethics

3 Sažetak

Naslov: Nekirurški estetski zahvati

Autor: Lara Sever

Sažetak:

Svačija želja je postati najbolja verzija sebe, posebno kada je u pitanju izgled, što je pokrenulo razvoj različitih estetskih postupaka.
U posljednje vrijeme osobito privlače pažnju nekirurški zahvati jer predstavljaju minimalni rizik te su pristupačni za pacijente.
Ovaj članak daje pregled najčešćih nekirurških estetskih postupaka koji se trenutno koriste, zajedno s razlozima njihove sve veće popularnosti.
Započet ćemo s ranim razvojem i napredovanjem, te sagledati bliže proces starenja kako bismo razumjeli promjene koje se kasnije rješavaju kroz tretmane. Spomenut ćemo najčešće moguće komplikacije te razmotriti tehnike liječenja boli koje se pacijentima nude kako bi se liječenje učinilo ugodnijim iskustvom. Konačno, ovaj pregled će raspraviti važnost pretproceduralne provjere pušenja, različitog pristupa kod muških pacijenata i uvid u etički aspekt nekirurških zahvata.
Da bi odabrali najbolji pristup za pojedinog pacijenta, moramo uzeti u obzir mnoge čimbenike kao zdravstveno stanje, jedinstvene anatomske karakteristike, kvaliteta tkiva, te njihova očekivanja kako bismo postigli najbolje rezultate.

Ključne riječi: nekirurški estetski zahvati, botulin toksin, dermalni fileri, deoksikolicna kiselina, kemijski pilingi, microneedling, laseri, nekirurška rinoplastika, liječenje boli, pušenje, muški pacijenti, etics

4 Introduction

Aesthetic procedures are becoming a growing field of medicine. The patient is generally well but desires an improvement of his or her appearance to enhance self-esteem (1) There are several factors contributing to increasing demand for those procedures, such as desire to prolong youthful look, economic abundance, technological and medical advances that enabled invention of new pharmaceuticals and devices which allow treatment with minimal recovery time and complications, professional compulsions to undergo aesthetic procedures as well as influence through media and high pressure advertising (2). However, the traditional surgical procedures are becoming less popular. Many patients do not want the cost, risk, and long recovery time that come with classical surgical procedures, so minimally invasive and non-invasive procedures offer them an alternative. Also, there is currently a trend to avoid the operated look (3). Nonsurgical aesthetic treatments are usually preferred because their effects are visible immediately after the treatment and patients can return to their normal activities on the same day.

This review will focus on the procedures that are mostly used today, as well as the complications that come along with them. Covered will also be the ways of managing the pain associated with the procedures in order to make them more pleasant for the patient. We will conclude with the hazard that smoking may pose as well as how to approach a male patient, which is a new and raising concern. In the end we will look at the subject from ethical aspect, as every physician in this field should be aware of it.

5 Aging and advancement of aesthetic procedures

Aging of the face is a dynamic process that involves soft tissue descent as well as deflation and loss of facial volume. In time the face loses both fat and volume and the skin loses collagen and elasticity. Full cheeks, present during the youth slowly turn into an aged hollowed face with bony contours and thin skin (4). The orbital aperture width and orbital aperture area increase significantly. This includes increase in height of the superomedial and inferolateral orbital rim. The glabellar and maxillary angles decrease, whereas the pyriform aperture area significantly increases. Mandibular length and height both decrease and the mandibular angle significantly increases (5). Epidermal thinning and the decrease in collagen cause skin to lose its elasticity. The deflation and loss of the normal anatomic subcutaneous facial fat compartments, coupled with gravity and muscle pull, leads to wrinkling and the formation of dynamic lines. These factors contribute to the formation of nasolabial folds, jowls, crow's feet, and the sagging appearance of aged facial skin (5,6). In addition to that, mandibular volume loss also affects the aging of the neck, as it may contribute to the increased laxity of the platysma and soft tissues of the neck. The increase in mandibular angle may result in blunting or the loss of definition of the lower border of the face. And blunted mandibular angle creates a loss of jawline definition (5). As the length and height of the mandible decrease, these bony changes result in the appearance of decreased chin projection that is found with increasing age (5).

Soft-tissue filler injections into discrete compartments, such as the deep medial, and middle fat pads of the cheek, have a significant effect on the soft tissues of the face, reshaping them into more youthful position (6).

They are used to successfully restore volume loss, most commonly in the anatomical regions of nasolabial fold, glabellar crease, malar region, nasojugal groove, and lips (7). As the majority of facial volume loss during aging is attributable to fat loss, the most ideal soft-tissue replacement could theoretically be fat (5).

The skin itself also goes through intrinsic changes over the years due to combination of some external and internal factors. Repetitive dynamic muscle contractions result in the appearance of superficial and deep rhytids over areas of habitual muscle contractions such as the orbicularis oculi and oris, risorius, frontalis, and corrugators because of fascial partitioning and connections of the dermis and periosteum between the different facial muscle groups (6).
Smoking and photodamage, resulting from sun exposure, lead to increased production of intracellular reactive oxidative intermediates and species and cause many facial skin changes resulting in epidermal thinning, solar elastosis, and dermal collagen disorganization, all this is then leading to characteristics consistent with aging skin (6).
Combination of facelift surgery with nonsurgical techniques of volumization, especially in the midface, is a common practice. Together they comprehensively address the effects of aging. Suspension of soft tissue and replacement of atrophy are both vital to facial rejuvenation. Therefore, when facelift is accompanied with volumization the procedure can result in significant improvements in appearance (4).
All of the commercially available and FDA approved fillers have only a temporary effect. These products ultimately resorb, which requires repeated injections for maintenance of the effects. For this reason, autologous fat transfer is a popular alternative (4).

The Papyrus Ebers, from the year 1500 BC, indicates that the ancient Egyptians were the first to document remedies that remain a part of our modern cosmetics procedures. They described the earliest forms of chemical peels, which included using sour milk baths for restoration of facial vibrancy. Later in the early 20th century, the modern techniques addressed skin laxity and descent through direct excision (8).
The idea of fillers for soft tissue augmentation has origins around the late 1800s. In 1893, Neuber described filling a depressed facial scar with fat transfer (9). Paraffin, a purified mixture of solid hydrocarbons from petroleum, was also used as a tissue filler. Prominent historical surgeons, such as Billroth, Gersuny, and Delangre were noted to use paraffin injections to treat

various deformities. In 1911, Kolle published a paper describing the correction of a saddle nose by paraffin injection. He also noted numerous complications, including severe granulomas, emboli, blindness, and even death (10). For this reason, paraffin as a filler fell out of favour by the 1920s. Silicone is yet another filler that has been used in the past, but has largely fallen out of favour due to its side effect profile and technique sensitive application (4). Nowadays several filler materials are no longer in use, however, there are still many options available for facial rejuvenation. These include collagen, calcium hydroxyapatite, poly- L-lactic acid, and hyaluronic acid products. Of these, hyaluronic acid fillers are among the most widely used due to their longevity, efficacy, safety, and most importantly, reversibility. Injection of hyaluronidase can be used if needed to breakdown the injected hyaluronic acid (11). This is particularly important in the rare cases of intra-arterial infiltration, as the consequences can be devastating (4).

6 Botulinum toxin-neurotoxin

Botulinum neurotoxins are produced from isolated Clostridium botulinum bacteria and work to induce muscle paralysis through inhibition of acetylcholine release at the neuromuscular junction (12). Each formulation of the available neurotoxins has a different mechanism to induce muscle paralysis, which is utilized for both cosmetic and therapeutic benefits (13).

The use of botulinum toxin type A (BTX-A) for cosmetics started back in 1998 when Carruthers and Carruthers (14) noted resolution of periorbital wrinkles in patients treated with BOTOX for benign essential blepharospasm. It is now the leading cosmetic procedure (3). Botulinum toxin rejuvenates the ageing face by reducing hyperkinetic lines associated with muscles of facial expression (15). At first it was used to relax dynamic lines and wrinkles, but further research led to discovery of broader BTX's versatility in cosmetic application. Today we can also use it for enhancement of the feminine eyebrow arch, lifting of the down-turned corners of the mouth or drooping

nasal tip, smoothening of a puckered, “pebbly” chin and reduction in gingival exposure in those with a “gummy smile”. (15)

We know seven distinct serotypes of botulinum toxin, those are A, B, C1, D, E, F and G. Serotypes A and B (BTX-A and BTX-B) are available commercially and the serotype most commonly used in the treatment of hyperkinetic facial lines is the serotype A. (15) BTX-A and BTX-B are composed of a heavy and a light chain. The heavy chain selectively binds the toxin to the pre-synaptic cholinergic nerve terminal. The light chain acts intracellularly to prevent acetylcholine vesicle release. After some time, collateral new nerve terminals start sprouting and eventually the original endplate regains function. Therefore, the inhibition of muscular contraction is only temporary (15). BTX-A can reduce hyperkinetic facial lines in glabellar region, crow’s feet lines and horizontal forehead lines. Efficacy of BTX-A and BTX-B was compared and it was found that although both are safe and effective, BTX-B has a more rapid onset and shorter duration of action, and may be associated with slightly more discomfort during injecting. Therefore, BTX-B may be used to treat patients who are refractory to BTX-A or show a reduced response to it (15). After BTX-A interferes with acetylcholine release at the neuromuscular junction (16) the muscle weakness becomes apparent in 2 to 3 days of the injection, with complete paralysis seen after 8 to 14 days. Muscles return to function approximately 2 to 5 months after injection, depending on the dose administered and the individual patient. However, patients receiving mean doses of 200 U are at an increased risk for the development of neutralizing antibodies (3).

6.1 Complications of btx injections

Side effects of BTX are usually related to high-dose therapeutic rather than cosmetic use (17). Adverse effects that can occur at any injection site include pain, edema, erythema, bruising headache and short-term hypoesthesia. Generalized side effects include malaise, nausea, influenza-like symptoms

and rashes (15). Muscle paralysis or muscle weakness is the aim of cosmetic uses of botulinum toxin, however, it can also unintentionally lead to an effect on surrounding muscles, as there may be local diffusion of up to 3 cm in diameter from the injection point (18). Local diffusion of the toxin from the procerus and corrugator supercilii muscles to the levator palpebrae superioris through the orbital septum can result in lid ptosis and diplopia (12,19) Ptosis in patients treated for glabellar rhytides can last for several weeks. Fortunately it is treatable and can be reversed with alpha adrenergic agonist ophthalmic drops (15). When injecting into or around the lip, there is significant risk for lip ptosis, as many muscles of facial expression are involved in the movement and shape of the lips. When injecting the mentalis, depressor anguli oris or orbicularis oris, unwanted spread or unintentional injection into the depressor labii inferioris may result in difficulty depressing the lower lip, resulting in an an abnormal or asymmetrical smile and in some cases even difficulty eating (13,20). Unintentional treatment of the zygomaticus major when treating the lower orbicularis oculi or over-treatment of the levator labii superioris alaeque nasi when treating “gummy smile” can also cause an abnormal smile, as these muscles control the movement and shape of the upper lip and lip corners (13,20). There have been cases where BTX-A injection was associated with the development of severe headaches lasting for up to one month. Patients may also experience dry eyes and superficial punctate keratitis, most likely due to toxin diffusion into the superomedial and superolateral orbicularis oculi, which leads to lagophthalmos and exposure keratitis. Injection site ecchymosis developed after less than 1% of all injection. Furthermore, they can be reduced by avoidance of medications with anticoagulant properties such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), herbal supplements such as vitamin E, gingko, smoking and alcohol for 7-10 days before the procedure (21,22). Cold compresses and direct firm pressure immediately after injection are also thought to reduce the risk of bruising after the injection. However, even with the use of proper technique and with careful patient selection, the periocular, perioral and lid margins, which consist of thin skin with superficial vessels, are very prone to ecchymosis (13).

Contraindications to treatment with BTX include pregnancy or breastfeeding, pre-existing neuromuscular conditions and concurrent use of some drugs such as aminoglycosides, penicillamine, quinine and calcium channel blockers (15,23).

The cosmetic application of BTX has revolutionized the medical aesthetics, and consequently made minimally invasive procedures much more popular. Cosmetic use of BTX injection is well established as safe and effective, with and there are also claims to suggest improvement in quality of life. The development of new products and different serotypes of BTX is leading to further advancements in this rapidly expanding field (15).

7 Intradermal fillers

Aging leads to loss of soft tissue which results in atrophic changes in the lips, exaggerated nasolabial folds and in some cases melolabial folds and marionette lines.

Although BTX is very effective in targeting dynamic lines and undesirable effects of hyperkinetic muscle contraction, it cannot restore the fullness that is lost with age, particularly of the lower part of face. However, the filler substances can restore facial fullness and smoothness and can be used in combination with BTX to provide longer-lasting results. Besides that, fillers also have a role in the treatment of acne scarring and facial lipoatrophy (15).

There is a substantial and growing number of injectable filling agents available. The ideal substance would be the one that is effective, has low risk of adverse reaction, has minimal recovery time and has long-lasting effects. Fillers can be broadly divided into three groups, based on their durability. First group are the biodegradable and non-permanent agents, examples are autologous fat, bovine collagen, porcine collagen, human collagen and hyaluronic acid (HA), second are semi-permanent agents, such as polymethylmethacrylate (PMMA) microspheres and calcium hydroxylapatite (CaHA) and the third group are permanent agents such as silicone (15).

The level of injecting the filler within the skin depends on the chosen area and the type of filler used. In broad terms fine wrinkles are treated with intradermal filler and deeper folds with filler in the deep dermis or subcutaneous space (15).

7.1 Bovine collagen

All patients that are treated with bovine collagen require prior skin testing. Most experts recommend two skin tests 2 or 4 weeks apart (24). Localized sensitivity is thought to occur in between 3% and 5% of tested or treated patients (15).

7.2 Human collagen

Human bioengineered collagen products do not require skin testing prior to use. There are several types available including Cosmoderm and Cosmoplast, both of which contain lidocaine and are FDA approved. The collagen is produced from a single line of human dermal fibroblasts. Cosmoplast is more resistant to degradation due to cross-linkage between lysine residues on the collagen and gluteraldehyde. It is indicated for deeper wrinkles and deep scars while Cosmoderm is indicated for superficial wrinkles. Duration of the effect is between 3 and 7 months (15,25).

7.3 Porcine collagen

Porcine collagen has only been recently introduced as intradermal filler. It is less immunogenic than the bovine one, although currently there is not that much data on its use as an intradermal filler (26).

7.4 Hyaluronic acid

Hyaluronic acid is a non-species specific substance. It is derived from either bacteria or rooster combs. Skin testing prior use is not required, although

several products contain hyaluronin-associated protein, which could create a theoretical risk for sensitivity reactions (27).
Side effects of hyaluronic acid are generally short lived and include erythema, bruising, induration and edema. Rarely, the patents reported the occurrence of delayed inflammatory reactions (15).
The effect of hyaluronic acid can be reversed by hyaluronidase, which can be used in case of excessive deposition or misplacement of hyaluronic acid, such as the Tyndall phenomenon, which is a “blue-bump” that results from excessively superficial placement of the dermal filler (28).

7.5 Polymethylmethacrylate (PMMA) microspheres

PMMA microspheres can be suspended with bovine collagen or hyaluronic acid, and this leads to stimulation of new collagen formation around the microspheres (15).
Skin testing for allergy to bovine collagen is required prior to use (15).
Short-term side effects include pain, redness and edema and long-term side-effect can be granuloma formation (15).

7.6 Calcium hydroxylapatite

Calcium hydroxylapatite is a semi-permanent filler. It does not require prior skin testing. It’s effect is supposed to last beyond a year (29,30).
Radiesse consists of calcium hydroxylapatite microspheres suspended in an aqueous carboxymethylcellulose gel carrier. The microspheres act as a scaffold for new collagen formation (31).
Side effects of Radiesse include erythema, edema and transient lumpiness (15).
This filler is not recommended for lip augmentation due to a high incidence of mucosal nodules (29).
It is as well not safe to be used for glabellar or periorbital lines due to the risk of necrosis or embolism (15).

7.7 Autologous fat

Autologous fat is a long-lasting volumetric expander used for structural grafting (32).
Autologous fat has been used for soft tissue augmentation for over a century. The advantages of autologous fat transfer are its lack of immunoreactivity and easy use of large volume (15).
Disadvantages include the need to extract fat for transfer, and variability in the viability of the grafted fat, which is supposed to be technique dependent. Harvested fat may be frozen for later use (15).
Harvesting fat via manual suction produces a high yield of pre-adipocytes with an intact stromal cell fraction (33). Neovascularization is necessary for transplanted fat survival, but stem cell differentiation and tissue fibrosis may also contribute to lasting augmentation (34).
Fat should be taken from an area that benefits the patient aesthetically, has a low risk for contour irregularities, and has the greatest potential for lipogenic activity (35). On women these areas are on the outer part of the thighs or on posterior part of the waists and on men the flank area. Fat should be extracted after tumescing with manual suction only, and then centrifuged. Small aliquots of fat are injected to keep injection pressures low during transplantation (3).
The most commonly encountered complications of fat transfer are ecchymosis, edema and contour irregularities (3).

7.8 Poly-L-lactic acid

Poly-L-lactic acid (PLA) is a biodegradable aliphatic polyester which is injected into the deep dermis or along the deep dermal subcutaneous plane. (2)
It provides an immediate temporary filling effect due to the physical presence of the reconstituted material.
Edema quickly settles and over the following weeks and months the material is metabolized, which results in dermal fibroplasia.

It has European approval for the correction of scars and wrinkles and FDA approval for the treatment of the signs of facial lipoatrophy in people with human immunodeficiency virus (HIV) lipodystrophy syndrome.
Pre-treatment skin testing is not required (15). Its duration of effect is usually from 12-24 months (36).

7.9 Silicone

Liquid injectable silicone is permanent soft tissue filler that is injected into the deep dermis or subdermal plane, there it induces fibroplasia and a gradual increase in tissue volume (15).
Liquid silicone for facial and body contouring became popular in the 1950s when it was believed to be inert, permanent and non-pyogenic. However, since then, many incidents have been reported in literature and in the media regarding cosmetic use of this filler (37).
Use of large quantities of impure silicone can lead to a number of serious complications including migration of the product, cellulitis and even death (38). However, judicious use of small amounts of pure liquid silicone (microdroplet technique) is supposed to have a low complication rate of as low as 1% (39).
It should be kept in mind that many of these devastating long-lasting complications come from injection of large volumes of industrial-grade impure products from either unlicensed or unskilled practitioners (40,41).
One of the complications of the procedure is siliconoma, which is granuloma formation due to reaction to silicone deposition. It can develop from several months to years after implantation (13) and can be treated with intralesional corticosteroid, oral corticosteroids and antibiotics (15).

7.10 Filler injections techniques

Firstly, the area of injection and the surrounding skin should be cleaned thoroughly. Then, anaesthesia is provided with topical lidocaine cream, which blocks regional nerves. The choice of injection technique depends on the location, its indication, the type of filler, and needle size (42). The techniques

include: linear threading technique, serial puncture, fanning, cross-hatching, depot, fern, and cone. The first four are used commonly and the last three are only used in specific situations. It is crucial to place the filler in the right location and the bevel orientation should not pose a significant issue at any site (43).

Full results of dermal fillers become apparent after 2 to 3 weeks, and the effects last anywhere between 3 months and 2 years. The duration depends on the type of filler used, where on the patient's face it was injected, how expressive the face is, and on the patient's metabolic rate. After repeated use of dermal fillers, many patients find that they have results that last longer than expected because hyaluronic acid-based dermal fillers stimulate the body's own collagen supply (43).
Patients are advised to avoid strenuous exercise on the day of treatment, to avoid drinking excessive alcohol within 2 days of treatment, and to sleep with their head elevated (43).

7.11 Complications of filler injections

In general, incidence of infection after filler injection is low. However, reactivation of herpes simplex virus may occur, therefore it is recommended to either use the prophylactic anti-viral treatment in people with known outbreaks or to postpone the procedure itself in those with active lesions (13).
Vascular occlusion is a rare but devastating consequence that can lead to tissue necrosis and permanent scarring, but is fortunately estimated to occur in only 0.001% of injections (44). Occlusion can occur due to compression of the skin's blood supply by excessive external filler material exerting pressure on the involved vessel, by venous congestion or by direct intra-articular injection (13).
The glabellar region is an extremely high-risk area due to the small, substantial vessels, the supraorbital and supratrochlear, that have little collateral circulation available in this area.
The alar grove is the location of the angular artery, which is a continuance of the facial artery and is so another high-risk area (13).

Techniques recommended to decrease the likelihood of this complication include aspirating before injection, using a small-gauge needle, minimising the volume of product used in one injection session, avoiding anaesthesia with epinephrine near a vascular bundle in order to prevent vasospasm and tenting the skin to avoid the vascular supply. Vascular occlusion must be treated emergently in order to give a chance of full recovery without serious long-term sequelae (13).

Most soft-tissue fillers are indicated for mid-to-deep dermal placement. So in case they are injected too superficially, complications such as visible product, nodule formation, hypertrophic scarring, and Tyndall effect can occur (45). Hypersensitivity and allergy to the product is nowadays considered a very rare complication when compared to the incidence seen in the past with collagen. Back then the high occurrence was contributed to not performing skin testing before the procedure. The original bovine collagen products became less popular due to the potential for allergic reactions and the need to perform multiple skin tests prior administration (46). PMMA is the only remaining filler which still contains bovine collagen, so it requires skin testing with 0.1 ml intradermal injection of collagen to the volar forearm 4 weeks before treatment. Patients testing positive, who develop either erythema or induration or those with two equivocal tests, who develop systemic reactions such as rash, arthralgia or myalgia, should withhold from the treatment (47).

Fillers have revolutionized the approach to facial augmentation because of their long-lasting correction with fewer side effects, greater lift, and the possibility of reversing unwanted aesthetic results (48). As more and more patients are choosing minimally invasive alternatives, the popularity of dermal facial fillers is rapidly increasing (43).

8 Deoxycholic acid

Deoxycholic acid is another injectable therapy. It aims to permanently dissolve fat in target areas (43). People are generally unsatisfied by excess fat under the chin or on the neck (49). Submental fullness creates an older and heavier impression, so reduction of fat in the area can consequently create a more youthful impression and also improve the contour of the jawline and chin (43). It is a non-invasive option that destroys fat cells, specifically in submental region (42) and it is affordable alternative to a submental liposuction (50,51). The effects are supposed to last a few years and may even possibly be permanent, particularly in the absence of significant weight gain. However, this has not yet been confirmed (49).
As with any procedure, complication may occur as well with deoxycholic acid. Those include erythema, edema, pain, numbness, bruising, and induration at the treated areas. More serious ones include dysphagia and marginal mandibular nerve injury (48).

8.1 Technique

During each treatment, the patient receives multiple small injections under the chin. The exact number of injections depends on the amount of fat under the chin and on the desired profiles. There must be at least 1 month in between each treatment session, with no more than 6 treatments in total (43).

9 Nanofat grafting

Autologous fat grafting was first mentioned in the early twentieth century (52). It became more widely performed after the introduction of liposuction by Illouz in the 1980s (53). One decade later the standardization of the fat grafting technique by Coleman followed and since then lipofilling has become a very important tool in plastic surgery (54,55). Adipose-derived stem cells were first discovered in 2001 (56). And since that, there was much research performed on these multipotent mesenchymal-derived progenitor cells.
The initial goal of fat grafting was to treat volume losses created by disease, trauma, or aging.

For this technique 27-gauge sharp needles are used. Therefore, the fat particles need to be sufficiently small. If the fat particles are too large, passage through the injection cannula is difficult. A disrupted injection follows, which may result in an unequal lipofilling with irregular fat deposits (57).
In order to ensure a smooth fat injection through those fine cannulas, the aspirated fat has to be processed mechanically to provide a liquid fat emulsion, which is now called nanofat.
In this emulsified fat the number of viable adipocytes is reduced, so the filling capacity of nanofat is consequently very limited.
Nanofat showed a capacity to improve skin quality after being injected, however, the exact mechanism of the regenerative effect on damaged skin is still not known. Improved elasticity is most probably due to increased collagen and elastin synthesis and remodelling. These effects are most likely initiated by stem cells rather than by grafted adipocytes. Especially as the adipocytes inside nanofat are supposed to be destroyed during the emulsification process.
It is impressive that these multipotent stem cells are richly present in fat tissue, as opposed to bone marrow or other sources of multipotent mesenchymal stem cells (58). Adipose-derived stem cells have an extensive proliferative capacity and the ability to differentiate into the mesoderm, ectoderm, and endoderm lineages (59-62).
As opposed to nanofat, classic fat grafting is mostly used to build up large volumes, especially in breast reconstructive cases. In those cases, it is crucial to preserve as many viable adipocytes as possible. Nanofat however, doesn't have the capacity to build up a significant fat volume is as such not suitable for those indications. Clinically it is used for skin rejuvenation procedures and is performed to correct superficial rhytides, scars, and dark lower eyelids.
The effect of nanofat usually appears with a delay of 4 weeks to 3 months, in contrast to faster effect seen in microfat (57).

10 Skin resurfacing

Resurfacing techniques treat skin surface irregularities, including acne, pigmentation disorders, actinic damage and changes caused by aging, such as wrinkling (63). Controlled injury in the proper depth is produced in order to treat the targeted pathology and to achieve the desired result (63).
Aging and actinic damage affect the epidermis and dermis. Aging causes epidermal hyperplasia, atrophy, and dysplasia leading to an atrophic and flat epidermis. Dermal connective tissue shows progressive diminution with great loss of the reticular dermis. Over time, collagen fibers become degenerated and thick. Less collagen leads to thinning of the skin. Aging also causes loss of dermo-epidermal papillae and melanocytes reduction. Actinically damaged skin exhibits elastosis, the presence of thickened, degraded elastic fibers (63).

There are different techniques available, such as lasers, chemical peels, and microneedling, which can lead to the stimulation of new collagen and elastin, the removal of abnormal tissue, and an overall rejuvenation of the skin. Multiple factors affect penetration and the depth of injury of each technique. Moreover, the risk of prolonged erythema or loss of pigment is directly proportional to the depth of resurfacing, and there is a possibility of experiencing prolonged healing times and scarring as well (63).

10.1 Chemical peels

Chemical peels have been used for decades already, for example in the treatment of acne or xanthelasma. They can be also used to rejuvenate photoaged skin. Peeling agents include alpha-hydroxy-acids (AHAs), trichloroacetic acid (TCA), Jessner's solution, salicylic acid, pyruvic acid and phenol-based formulas (15).
Chemical peels create an injury in a specified skin depth with the aim of stimulating new skin growth and improving surface appearance and texture (64).
There are 3 basic types of chemical peels. Superficial peels (glycolic and salicylic acids) can penetrate to the papillary dermis. Medium-depth peels (trichloroacetic acid) reach the deep papillary and, often also down to

superficial reticular dermis. Deep chemical peels (phenol) can penetrate all the way into the midreticular dermis (3). We can choose the depth of the peel required, after we assess the location of the pathological process. Superficial peels are used to improve appearance of the skin, medium depth peels treat superficial wrinkles and pigmentary changes, while the deep peels are able to treat deep wrinkles, but are associated with significantly longer recovery times (65,66).

10.1.1 Complications of chemical peels

Risks of chemical peels are most of the time directly proportional to the depth of the peel. All peels can cause pigmentary changes. However, deep peels using phenol can result in depigmentation and scarring can result from either medium and deep peels. Bacterial infection or reactivation of herpes labialis can occur with any peel. Prolonged erythema, defined as an erythema lasting beyond 90 days for deep peels, and milia formation may also result from any peel (67). Minor complications include irritation, burning, erythema, pruritus, edema, and blistering (64). Major complications are usually rare and include allergic reactions, laryngeal edema, toxic shock syndrome, cardiotoxicity, salicylism, acute kidney injury, lower lid ectropion, corneal damage, significant scarring, and dyspigmentation (64). Acne may occur during the re-epithelialisation process and can be treated with topical and oral antibiotics, topical azelaic acid, low-dose intralesional corticosteroids or low-dose isotretinoin (13). Deep chemical peels such as phenol necessitate specialised care such as cardiopulmonary monitoring, as phenol can enter the circulation resulting in cardiotoxicity (68).

10.1.2 Combination treatments

Chemical peels can be combined with other nonsurgical cosmetic procedures including botulinum toxin and fillers. However, botulinum toxin injection should be performed 2 weeks before the peel treatment with similar or later timing for temporary fillers (66).

Following is a short description of the most commonly used chemical peels.

10.1.3 Alpha-hydroxy-acids

AHAs are naturally occurring carboxylic acids, which are derived from fruit and vegetables. Glycolic acid is the most commonly used AHA peeling agent and was found to increase epidermal thickness, epidermal and dermal hyaluronic acid and collagen gene expression when applied to forearm skin twice daily for 3 months as a 20% Glycolic acid lotion (69).

10.1.4 Salicylic acid

Salicylic acid 30% in a hydro-ethanolic vehicle is used as a superficial peeling agent. Side-effects included stinging and burning during the procedure, and superficial crusting, edema and transient purpura after the procedure (70).

10.1.5 Pyruvic acid

Pyruvic acid is an alpha-keto-acid that converts to lactic acid. It can be used as a medium-depth peeling agent in the treatment of photoaged skin (71).

10.1.6 Phenol peels

Phenol peels are deep peeling agents and produce significant destruction of epidermis and upper dermis. Patients require counseling before treatment regarding post-peel edema and necrosis, as complete re-epithealization can take up to 10-14 days (15).

10.2 Microneedling

Microneedling is a procedure in which thin needles are rolled over the surface of the skin to induce rapidly healing micropunctures. The production of these microwounds initiates the postinflammatory chemical cascade and ultimately stimulates collagen production. Increased collagen production paired with elastin fiber production results in skin remodelling (72).
Microneedling is used to treat wrinkles caused by skin aging, for scars, and for treatment of stretch marks as well (72,73).

Many patients prefer microneedling to laser and chemical peels because it is safe for use in all skin tones, all parts of the body, including abdomen stretch marks, and allowed at all times of life, including pregnancy and breastfeeding. Because the epidermis is retained, microneedling carries lower risk of infection, postinflammatory hyperpigmentation, and scarring compared with other resurfacing techniques (64).
Moreover, the recovery time with microneedling is short, with mild redness usually lasting less than a day, as compared with 1 week or more with laser or peels (43).

10.2.1 Technique

Firstly, topical anaesthesia with lidocaine and prilocaine cream (EMLA) is applied to the area to be treated and covered with cellophane tape for 15 to 45 minutes. After removal of the cream, antiseptic solution is applied right before starting the procedure (72).
The skin is stretched by one hand and the other hand is used to roll the instrument over in a direction perpendicular to that of stretching force. The roller is rolled 15 to 20 times in horizontal, vertical, and both oblique directions. The base of the scar should be treated and the pinpoint bleeding should occur from it. Saline pads are placed over (43)
The treated area becomes swollen and superficially bruised. It should be covered with damp swabs, which are replaced every 2 hours to absorb the bleeding and serous discharge. Topical antibiotic cream should be applied for a few days to minimize the chance of bacterial infection. Patients should avoid sun exposure and strong chemicals or any facial cosmetic procedure for at least 1 week (43).

10.2.2 Complications of microneedling

Complications of the procedure are very rare. One example would be the consequence of usage of poor-quality needles on the roller device, which can

lead to bending at needle tips after multiple treatments, and this can result in more tissue damage (43).

Microneedling is an alternative option for patients who are unwilling to try neurotoxins or fillers but still desire an improvement of their skin complexions. Skin appearance is improved almost immediately and continues for 4 to 6 weeks. Overall, the microneedling is a painless skin resurfacing option with minimal chemical exposure and short recovery time (43).

10.3 Lasers

Another form of skin resurfacing, the laser resurfacing, can be used to treat freckles, melasma, age spots, and fine lines around the eyes and mouth. Laser treatment can also be combined with surgical procedures, such as a facelift or blepharoplasty (43).
High-energy light pulses are sent out from the laser. Those are then absorbed by water and chromophores, which are substances in the skin. The light from the laser transforms into heat energy, which then targets small sections of the skin, layer by layer (43). The healing process follows, during which new skin grows to replace the skin treated by the laser (74).
The ablation depth of lasers is strictly controlled and there are two types of lasers available, characterized as either ablative or non-ablative (75).
Ablative lasers vaporize the superficial layers of the skin by heating the dermis to stimulate new collagen production by fibroblasts (76). Ablative lasers commonly use pulsed carbon dioxide and erbium:YAG laser wavelengths (75). On average, carbon dioxide systems ablate 20 to 60 mm of tissue with the initial pass, and the residual thermal damage extends to a depth of 20 to 100 mm after multiple passes, making them more useful for deep ablations (75).
The erbium:YAG pulse lasers vaporize 2 to 5 mm of tissue per pass and leave behind a 20- to 50-mm zone of residual thermal damage, so are mostly used for finely tuned light to medium ablations (75).

Goal of these laser systems is to produce a significant degree of improvement with less skin wounding to generate fibroplasia and granulation but with thin zones of thermal damage (75).
In contrast, nonablative lasers only create focal thermal injury within the dermis and this way stimulate collagen growth (75). The Q-switched neodymium:yttrium-aluminum-garnet laser is particularly a good option when treating periocular and perioral rhytides (75). Other nonablative lasers include intense pulsed non-laser light sources, diode lasers, and pulsed-dye lasers (75). Fractional photothermolysis induces deep dermal damage that stimulates collagen synthesis and remodelling and at the same time produce minimal epidermal damage (75). The laser procedures require only a short recovery time and the treated skin looks rejuvenated after 2 weeks. However, treatment may require several sessions (75).
An extensive knowledge of skin histology is required in order to be able to practice laser resurfacing. Laser treatment should be considered as a principal noninvasive option in patients seeking significant improvement of their facial complexion (43).

11 Non-surgical rhinoplasty

About a century ago Rebert Gersuny and James Leonard used liquid wax made from paraffin to correct saddle nose (43). Decades later, microdroplet silicon injections on multiple sessions were introduced by Robert Kotler and Jack Startz. However, due to high rate of granuloma and ulcer formation the idea lost its popularity (77,78). The era of polyacrylamide injection also encouraged some physicians to inject it in the nose (79).
Nasal units, angles, facial aesthetic proportion with the nose, and all facial units are making harmony in human facial look and should therefore be considered when performing rhinoplasty (80).
Firstly, big proportion of clients is not willing to undergo surgery and general anaesthesia either due to psychological or physical factors (81). Secondly, advantage of non-surgical rhinoplasty are postoperative minute deformities

(82). Non-surgical rhinoplasty can also be performed as a pre-operative temporary corrective plan to enable surgeon to judge if his planned surgery could meet patient's expectations (83).

Non-surgical rhinoplasty with fillers has in the past few years shown to be an effective alternative for patients seeking only an aesthetic improvement of the nose (84). However, use of fillers, Botox, or thread cannot achieve precise correction in cases of big nasal deformities (82), so this is not actually an alternative for surgery. Therefore, if there is any significant nasal deformity, either in rotation, projection, saddling, tip width, septum, or bone, it needs to be corrected by surgery and this totally agrees with Pontius et al. (85).

Most popular and most commonly used among fillers are the hyaluronic acid fillers. This could be attributed to the easiest technique of hyaluronic filler injection when compared with calcium hydroxylapatite and the wide varieties of its application, in nasal tip, supratip, infratip, columella, side walls, nasolabial groove, frontonasal angles, and it could be injected easily anywhere in the nose either touching dermis, or on cartilage when indicated to correct cartilaginous deformity (83). Calcium hydroxylapatite is less soft and it works well when injected deeply over the bone and is used to augment the dorsum (83). It could last for about 3 years in contrary to the HA duration which is around 6 months (83).

The frontonasal angle, nasolabial angle, nasofacial angles can all be markedly improved to reach near normal measurements (83).

Saddle-nose deformity, supra tip depression, infratip lobule depression, alar irregularities, domal definition, clomellar lengthening, can all be corrected by fillers (83).

Tip definition, rotation, alar flaring improvement and bunny lines elimination are highly achieved by Botox. Thread can achieve a measurable improvement in nasal saddling, tip narrowing and reduction of the nasal base (83).

11.1 Complications of non-surgical rhinoplasty

There is a number of complications that can occur during non-surgical remodelling, including Botox over-dose, infection, ischemic necrosis from

arterial embolism, pressure necrosis from over-injecting the nasal tip, and osteophyte from periosteal injection (86).

However, the most catastrophic of all complications that can happen due to rhinoplasty with fillers is blindness (86,87,88). But this can as well occur in other facial filling procedures with fat (88) or hyaluronic acid. Fortunately, it can be avoided by proper precautions during injection, especially syringe aspiration, withdrawal injection, and avoidance of high-pressure bolus injection (83).

The hypothesis behind blindness is based on the presence of an anastomosis of the nasal area, consisting of a dorsal nasal artery from the ophthalmic artery, an angular artery, and a lateral nasal artery from the facial artery. Li et al. (89) concluded that injection into nasal dorsum may accidentally break into the anastomosis, resulting in retrograde embolism of the ophthalmic and clinical blindness for the patient. Liew et al. (84) also underlined the importance of a good knowledge of standard vascular supply and its variant is essential to avoid vascular complications not only represented by blindness but also by nasal skin necrosis.

The dorsal and external nasal arteries are also branches of the ophthalmic artery, which also provide collateral flow to the nasal tip. Isolated reports of tip necrosis have occurred following the use of fillers of all types, and it has been documented as a rare complication of surgical rhinoplasty (84). The mechanism behind this is assumed to be compression, occlusion or embolization of these vessels. These events are clearly not unique to the nasal vasculature, with similar reports seen following administration of fillers in the forehead, glabellar, temple, and the nasolabial region (87,90,91).

Withdrawal aspiration, before injection must be performed and that could be the safest step before injection, to avoid intravascular embolus, and subsequent blindness. Injection techniques for fillers are differing among physicians, but the most important consideration is to avoid intravascular injection (83).

Antiseptic technique with proper sterilization, careful handling, and withdrawal precautions during any injection, should be emphasized. If blindness (86) is diagnosed, immediate reperfusion management by ophthalmologist should be started, using all tools such as dissolving hyaluronidase injection,

corticosteroids, diuretics, oxygen, nitropaste topical application, hyperbaric oxygen, carbogen, and lysis therapy (87,92,93).

12 Pain Management

12.1 Botulinum toxin

As botulinum toxin injections are the most frequently performed cosmetic procedure in the world, there is a great interest in making this procedure as painless as possible (94). Technique using extremely fine needles of 30 gauge or smaller has been proven to decrease discomfort (95,96).
The use of ice, cold packs, or topical cooling devices before injection can also decrease pain and bruising (97-100). Topical anaesthetics were found to decrease pain in up to 100% of patients in many of studies, but they were comparable to the effects of topical skin cooling (99, 101,102). Vibration devices are usually less commonly used, but have also been described to reduce injection site pain in 82% of patients (103). Even oral analgesics or anxiolytics could be used before botulinum toxin injections, but it is not a common practice (94). There have been some reports of mixing lidocaine with botulinum toxins, however, the manufacturers do not recommend this (94).

12.2 Fillers

Pain control for filler injections is similar to botulinum toxin injections, but there has been more research on addition of lidocaine to these products before injection (94). Techniques that are believed to decrease discomfort before filler injection are use of smaller needles, slow injections, vibration, contact cooling, and topical anaesthetics (101,104,105). Vibration was observed to be more comfortable for 95% of patients and contact cooling provided 61% pain reduction and 66% less ecchymosis (94). Mixing lidocaine with injectable has been found to decrease pain, but it as well changes the viscosity and characteristics of the filler (106-111). However, this does not significantly change the final results of the procedure (111).

Calcium hydroxylapatite was the first filler to receive Federal Drug Administration approval for mixing lidocaine with the filler before injection (106,111). Poly-l-lactic acid is also a filler, which is frequently mixed with lidocaine. Currently, most hyaluronic acid products available on the market include pre-mixed lidocaine, at least as an option (94).

Finally, the use of blunt needles or cannulas for filler injection was described in some studies. These studies claim cannulas decreased pain, bruising, and edema relative to use of a traditional needle (112-114). Generally, small gauge needles are used when possible, 32 gauge for neurotoxins and most often 27 or 28 gauge for fillers (94).

For neurotoxins, patients are given the option of application of topical analgesics, however many defer this option. For fillers, patients are also given the option for topical analgesia, but the premixed lidocaine versions of these products is generally preferred (94).

As with any procedure that potentially leads to pain or anxiety for a patient, it is important to assess patient's pain tolerance prior to the procedure, to determine the level of intervention needed (94).

13 Smoking

Nicotine is the principal vasoactive constituent that induces endothelial wall damage, inhibits capillary blood flow, and releases catecholamines (115). Carbon monoxide is another major component that competitively binds to haemoglobin, thus reducing the oxygen-carrying capacity of blood (116). However, nicotine-induced vasoconstriction and carbon-monoxide-induced diminished tissue oxygenation are partially reversible within a few days after smoking cessation (117-119). In addition to that, improvement of inflammatory healing response and oxidative bacterial killing mechanisms are also achieved by smoking cessation. This consequently leads to reduced infections, after 3 to 4 weeks of abstinence from smoking (118,120,121). Therefore, majority of plastic surgeons recommend smoking cessation for at least 4 weeks before and after most elective aesthetic procedures (122).

Smoking status of the patient should be evaluated by the physician, before performing the procedure. Whenever in doubt, physician can perform quantitative cotinine assays to estimate the risk for potential malperfusion (123). Cotinine is the major metabolite of nicotine. It is also a specific biomarker for nicotine exposure in cigarette smokers. There are two types of the test available for measuring the concentration, the salivary and urinary cotinine test, and both are equally efficacious (124,125). This is especially important when dealing with patients who have had previous surgical interventions, such as rhinoplasty or face lifts, and have therefore potentially altered vasculature (123).

Pre-procedure questionnaires about smoking are also an option, however there were many cases of underreporting of the number of cigarettes that the patients smoked daily. Which was later on proven and quantified by biochemical measurements. This is especially an issue when dealing with patients who claim to have quit smoking, therefore performing a cotinine screen is the safer option (126).

Counseling about smoking cessation may be discouraging for some patients, however, it is still believed to be one of the most powerful tools to convince a smoker to quit. It will also help patients to make better decisions and set realistic expectations regarding the results of the procedure (126).

14 Aesthetic procedures on men

Significant anatomical, physiological, and behavioural differences are present in the aging face of a man in comparison to woman, and all those require specific considerations when performing aesthetic treatments (127). For example, men have more skeletal musculature than females and this as well extends to mimetic musculature given that men have more facial muscular movement than women (128). This consequently leads to the fact that men usually have more prominent dynamic facial rhytids than women (129) except for the perioral area(130). Skin in males is generally thicker and has a higher collagen content than in females (131) and this is also true for the facial skin.

Men also tend to have more sebaceous skin and may therefore more commonly seek treatment for sebaceous hyperplasia. Men have greater vascularity and perfusion of facial skin, which may carry a greater risk for complications of aesthetic procedures (132), such as bleeding and bruising. There are also gender-specific differences in facial bone structure. Men have a more prominent supraorbital rim, a larger forehead, and flatter cheeks that are more angular (133). Men also have a greater forehead slope from brow to hairline, a flatter brow, and a more defined hairline with a wider and more forwardly projected chin (134). These anatomic differences are of great importance and need to be considered when planning aesthetic procedure. As exaggeration rather than restoration of typical male features can result in an aggressive or threatening appearance, whereas accentuation of feminine features will have a feminizing effect (134) .

After gender-specific anatomical and physiological considerations, behavioural and psychological factors must also be considered before performing a procedure on a male patient. Men find facial symmetry desirable, just as women do (135). However, men often do not desire complete eradication of dynamic rhytides, but prefer to have them softened instead (134).

Men still consist just a minority of patients who are seeking aesthetic procedures, so they are less likely to have heard about specific procedures from others. Therefore, new male patients might require more counselling than females would (127).

15 Ethics

Whenever treating patients, especially in the field of aesthetic procedures, we also need to consider their psychological state.

Dysmorphophobia is an underrecognized and underreported condition in aesthetics. Commonly there is a fine line dividing the desire and the obsession. Aesthetic surgeons need to be cautious and should recognize this condition in order to manage it effectively or refer these patients appropriately,

instead of just unethically continue performing multiple procedures. (136). There is not much information and knowledge available that would help detecting these disorders by dermatologists and plastic surgeons, and most patients never reach the psychiatrist (137). In case patients are seeking repeated procedures for minor defects, the physician must refer them to the psychiatrist for appropriate treatment, in order to practice ethically. Such patients do not have realistic goals and are likely to be always unsatisfied and unhappy, regardless of the treatment outcome (136).

16 Conclusion

There is a wide range of nonsurgical aesthetic procedures available. Overall, these procedures aim to optimize facial aesthetics by enhancing symmetry, augmenting facial contours, improving proportions of the face and neck and creating youthful appearance, everybody strives for (43).
From more traditional reduction of the wrinkles by botulinum toxin, there are many other new techniques emerging rapidly. A more recent discovery of facial fat compartment anatomy has revolutionized the concept and approach of adding volume to specific deflated soft-tissue compartments, creating a more individualized youthful restoration to the face. Soft-tissue fillers have an impressive ability to volumise and reshape ageing, sagging skin within a short time and with minimal side effects (15).
Hyaluronic acid fillers are most commonly used filler due to their longevity, efficacy, safety, and most importantly, reversibility. However, most of the effects of the fillers are only temporary, and this is where autologous fat transfer comes as an alternative, with its permanent effect (15). Nanofat transfer is a new variant available, however due to little particles is not able to build up significant volume and is only used to correct superficial rhytides, scars, and dark lower eyelids (57).
Deoxycholic acid is a non-surgical way to permanently dissolve fat and so improve the contour of the jawline and chin, which helps create a more youthful appearance (43).
Patients looking for improvement of the surface of their skin either regarding changes caused by aging, acne, or pigmentation differences, are good candidates for skin resurfacing procedures.
Chemical peels, lasers and microneedling produce a controlled injury that must be of the proper depth in order to treat the targeted pathology and achieve the desired result (43).
Non-surgical option of rhinoplasty using fillers, such as hyaluronic acid, is able to correct minor nasal deformities. The effect lasts only temporary but is a good alternative for people not wanting to undergo surgery and general anaesthesia (83).

An important factor to consider before performing the procedure is definitely smoking status of the patient. Tobacco use has been shown to not only be a causal factor for numerous chronic diseases, but also an independent risk factor for several surgical and wound healing complications (122).
When it comes to pain management, the assessment of patient's pain tolerance should be done in advance to determine the intervention needed. Use of ice packs, topical cooling devices, vibration devices and topical anaesthetics have all been shown to decrease the pain to some extent. Fillers are most commonly available pre-mixed with lidocaine (94).
Lately, aesthetic procedures gained a lot of popularity also amongst males. Therefore, physicians performing nonsurgical aesthetic procedures on male patients should be aware of anatomical, physiological, behavioural, and psychological factors that are unique to them (127).
Physicians should be trained to recognize patients with dysmorphophobia, because continuing procedures on those people will most probably lead to more harm than good (136).

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20 Biography

I was born on 03.07.1995 in Slovenia. I went to primary school and high school there. After graduating high school in the summer of 2014 I enrolled into first year of the Medical studies in English at the School of Medicine, University of Zagreb that autumn. During my studies, I was a student demonstrator for Anatomy for two consecutive years. I was a member of the Faculty of Medicine rowing team for 6 years and I have participated in many national and travelled to many international regattas throughout these years. I have also been a part of the students' organization CROMSIC. I have participated in and organized several events there. In the August of 2019 I took part in an exchange to Brazil for a month. I got another exchange this year when I am supposed to travel for a month to Peru. In Brazil I did a research program, which helped me expand my knowledge in laboratory work, and this year in Peru I am about to do a clinical program at the hospital, to gain more experience there.

This year I took part in the BHFTA 2020 event where, together with my classmate, we prepared a poster. During the April of 2020 I was supposed to complete one month rotation at McGovern Medical School, University of Texas, Health Center at Houston in the cardiology department. Unfortunately, it was cancelled last minute due to the Covid-19 situation. Furthermore, I was supposed to complete rotations at several departments at the University Hospital KBC Rebro in Zagreb during May and June 2020, which got all cancelled for the same reason.

I will graduate in July 2020.