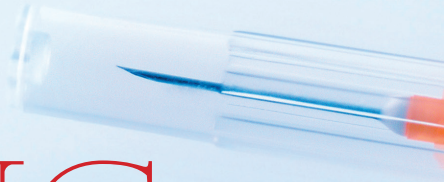
WHERE ARE WE GOING WITH VOLUMISING INJECTIONS?



Dr Joan Vandeputte reviews the current and future role of fillers in aesthetic medicine, including indications, potential problems and areas for further research

COVER STORY

ABSTRACT

The number of indications for volumising injections is increasing. Fillers continue to be developed for direct volume substitution, biostimulation or a combination of both.

Representative clinical cases, pictures from cadaver dissection after the injection of a dyed filler, and data from the literature are used to review indications, assumptions and potential problems and to highlight points of interest for clinical training and further research.

Injected amounts vary from precise corrections requiring less than 1 ml to comprehensive treatments with tens of millilitres. No single product is suitable for all indications.

Product characteristics, tolerance, safety, complications and patient satisfaction are described extensively in the literature. Little has been published on the histology of filler behaviour and tissue response. Assumptions are made about filler deposition during injection and remodelling by pressure. We lack quantitative data on resulting volume per injected amount, on resorption versus time and on reactive oedema.

Because of the relatively high-risk profile and the complexity of volumising injections, extensive training, including cadaver dissection, observational and hands-on training, and gradual progress from lower to higher risk and complexity treatments are highly recommended.

GENERATIONS OF PLASTIC SURGEONS have considered the removal of obvious bulges and the treatment of sagging as principal paradigms in facial rejuvenation. The strategies came down to excision and shifting of soft tissue volumes. Over the last decades, the treatment of volume deficiencies by fat injection at various levels of depth[1] has successfully expanded the armamentarium. In parallel, fascinating techniques were developed by non-surgical and surgical colleagues to compensate volume loss by injection, at various levels, of fillers, some of which are biostimulatory[2,3].

Besides the hollow eyes and tight-pulled faces resulting from surgery[4], chipmunk cheeks, extravagantly pouting lips and inflated faces have now also appeared in our communities, on occasion also in professionals in the field of medical aesthetics.

While the numbers of indications are expanding along with the number of therapeutic options, achieving a predictable outcome, avoiding excesses and accurate risk management remains a challenge.

Materials and methods

Representative clinical photography from the author's practice and of his cadaver dissections were compared to data from the literature, reflecting on the evolving place for volumising injections in facial aesthetics and points of interest for studies and clinical training. The author chiefly used the following fillers.

The Belotero* portfolio consists of non-particulate hyaluronic acid (HA) gels. The Restylane** portfolio comprises particulate HA gels. All are derived from bacterial HA and cross-linked with 1,4-butanediol diglycidyl ether (BDDE). The cellular tissue response is low. After hydrodynamic and enzymatic break-down locally, endogenous HA is metabolised in the lymph nodes, the liver and the kidneys while a small portion is excreted in the urine[5]. HA gels probably follow the same pathway in a delayed manner. Clinical and MRI studies ▷

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KEYWORDS
L-Polylactic Acid, Calcium Hydroxylapatite, Hyaluronic Acid, Agarose, Volumising injections, Fillers, Face, Facial Rejuvenation

“Representative clinical photography from the author’s practice and of his cadaver dissections were compared to data from the literature, reflecting on the evolving place for volumising injections in facial aesthetics and points of interest for studies and clinical training.”

Figure 1 This 43-year-old lady was treated mainly for early signs of aging (forehead flatness, show of temporal crest, decreased cheekbone prominence, cheek hollowness, diminished visibility of the jawline, early jowling) and also for a constitutionally slightly retruded chin. (A) Before the treatment. (B) Injections. Purple: HA (Belotero Volume), close to bone. Orange: HA (Belotero soft), close to bone. Quantities in ml. White lines: 1.5 ml of calcium hydroxylapatite (Radiesse) compounded with 0.3 ml of Lidocaine 2% per side, subdermal. (C) Result three months after the second session. (D) Result one year and three months after the second session. There is still a visible effect in all treated areas except the forehead.

▷ show HA gels to stay in situ for years[6,7] after deep injection.

The Algeness*** portfolio are particulate gels of agarose from Gelidium red algae. The purified agarose is not chemically modified. The local cellular response is high, as the filler is resorbed in situ by macrophages without capsule formation. Little has been published on the longevity of results. The author observed clinical effects that lasted well over a year.

Radiesse**** is a suspension of calcium hydroxylapatite microspheres in a carboxymethylcellulose gel. The gel is resorbed in a few months, while the biostimulatory effect of the resorbing spheres, inducing microcapsules, last for over a year[3].

Sculptra***** is a powder of a poly-L-lactic acid (PLLA) polymer, suspended in water for injection before use. It has a strong biostimulatory effect by encapsulation and fibroplasia. As it is slowly resorbed, it is categorised as a semi-permanent filler[3].

Results and discussion

Applications for volumising fillers

Volumising fillers can be used to compensate for acquired or constitutional bone or soft tissue volume deficiency (*Figure 1*). Increasing projection (e.g. eyebrows, cheekbone, mandibular angle, chin) may require more focal deposition of filler, while diffuse filling of excessive concavity and smoothing of sharp surface boundaries requires even deposition over larger surfaces.

Volumising fillers can also provide support to overlying structures. The treatment of a slightly drooping nasal tip (*Figures 2-3*) is a typical example.

Safety

The most frequently reported severe complication of fat or filler injection is necrosis[8,9], followed by a worrying number of cases of blindness[8-11]. The highest incidence among fillers is reported for HA[7,8], but this is also by far the largest group by number of injections[12]. Preventive measures and recommendations for treatment were listed extensively by Belaznay et al[11]. Infections of injected areas and granulomas[8,13], if less catastrophic, are still serious although less rare complications.

HA's have the distinct advantage that they can be removed fast from the interstitium by hyaluronidase injection. To some extent, intra-arterial HA can be dissolved by hyaluronidase injection in and even around the vessel[9].

Where is the filler going during injection?

Comparison of MRI to dissections in 40 cadaver heads, after injection with MRI contrast medium mixed with food dye, by Cotofana et al.,[14] showed no displacement of filler outside the intended area of injection. However, work by Pilsl et al.,[15] indicates otherwise. They injected the premaxillary (Ristow's) space in 15 cadaver heads with calcium hydroxyapatite in carboxymethylcellulose versus a less viscous dye designed for intra-arterial injections for anatomical dissections. The dye spread into the malar fat pad (the deep medial fat pad). They concluded that the premaxillary space is semi-open. Pavicic et al.,[16] demonstrated, in a cadaver study, that needle calibre and, even more, angle of injection, influence filler spread along the needle trajectory. *Figure 4* confirms how a filler, injected perpendicular into the temporal muscle, can spread to a superficial level.

> "The most frequently reported severe complication of fat or filler injection is necrosis, followed by a worrying number of cases of blindness."

Cannulas can distend septae which, on retraction, shift the injected bolus to a more proximal position along the trajectory[17].

We can therefore not take for granted that all filler is deposited exactly where we intend, nor that it cannot spread instantly in an undesirable direction.

Where is the filler going after the injection?

The ideal volumising filler would not migrate under external pressure and resume its original shape when the pressure is released. While its elasticity can be measured *in vitro*, we do not know yet if filler rheology has a measurable impact on the elastic behaviour of injected tissues.

Although remodelling of the injected zone by finger ▷

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Figure 2 This 42-year-old lady was injected with agarose (Algeness HD 1.5%). A syringe of 1.4 ml was compounded with 0.2 ml Lidocaine 2%. 1 ml was injected in between the medial crurae of the alar cartilages and the anterior nasal spine, so as to provide a stiffer and higher pillar supporting the tip. A deposit of 0.3 ml on the intermediate crurae further augmented the tip (A) Situation 4 days after administration of 4 units of incobotulinum toxin A to the depressor septi nasi muscles and before filler injection. (B) Result after 3½ months.

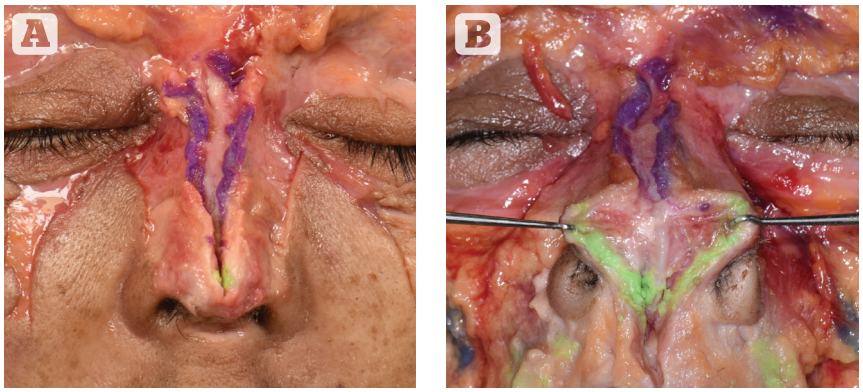

Figure 3 Cadaver dissection after linear retrograde injection of dyed 1.5 % agarose gel (Algeness HD) (purple) on the nasal dorsum and of 2.5% (Algeness VL) (green) in between the alar cartilages, linear retrograde, with a 25G cannula. (A) The filler on the dorsum is not only located in between the periosteum or perichondrium and the musculature. It also penetrated into both layers, with a tendency to be more superficial far from the entrance point at the nasal tip. Tip augmentation is visible in green on the intermediate crurae. (B) Filler injected in between the medial crurae beginning at the anterior nasal spine can stiffen tissues sufficiently to create a pillar that pushes the tip of the nose forward and upward.

▷ pressure is common practice and described in the literature[6,18], we need more research to find out if external compression can effectively do more than change the shape of the deposit without displacing it and expulsing a reactive oedema. Cadaver dissections after injections with dyed agarose gel showed no apparent effect of firm remodelling (*Figure 5*).

Lumps and swelling

Lumps, besides cases of infection or granuloma, can originate from the irregular deposition of filler, water absorption by the filler, reactive oedema or tissue response with cellular components, with or without capsule formation.

A contour deformity can only be focal. A good example is a small, unintended, subdermal deposit occurring during deep injection on the orbital margin. The thin skin of the temple does not easily hide irregularities. Lambros advocated diluting hyaluronic acid dermal fillers with saline for subcutaneous, temporal injection because of the high probability of lumps in this area[19]. A deformity can be local, including the entire filler deposit and the immediate vicinity, such as sometimes happens after HA injection over the orbital margin. Third, contour deformities can also be locoregional, such as oedema in the wider surroundings of the injectable, with a puffy look.

Precision and predictability

To avoid clogging of the needle by particles, poly-L-lactic acid suspensions need to be prepared well in advance and at sufficient dilution[3]. The product has to be spread out as evenly as possible throughout the target area to avoid the formation of visible and palpable lumps, with a higher dilution for subcutaneous than for deep treatment. The low viscosity and the imperative diffuse spread make it less suitable for circumscript corrections. The biostimulatory effect is strong, but the result depends on tissue response, which takes time and, like any biological phenomenon, is variable.

The viscosity of calcium hydroxylapatite and the more subtle tissue response makes it more suitable for circumscript corrections, while diffuse infiltration can be performed just as well. The result at mid and long term is not uncommonly appreciated more after a repeat treatment. Immediate reactive oedema can be pronounced, but mid- or long-term oedema is very rare.

It is not recommended to inject biostimulants in the glabella, on the orbital margin, in the lips or in the nose because of the risk of direct visibility of hard lump formation and for safety reasons.

The vast array of HA gels offer great versatility in subcutaneous to deep injection, to increase projection or for diffuse filling. Reactive oedema immediately after injection is limited but mid- and long-term oedema, especially in the periorbital area and the lips, can be an issue. Soft irregularities may occur, especially in areas with thin skin[19]. In some individuals there is some loss of projection over time and some volume increase extending beyond the injected areas (*Figure 6*).

Agarose is suitable for increasing projection and support and for diffuse filling. It gets surrounded by histiocytes within hours after injection. This may help to maintain projection and support. The tissue response may become palpable and visible if concentrations higher than 1% get into contact with eyelid dermis or 1.5% with other dermis. The response to deeply injected 3.5% is sometimes palpable for several weeks. Reactive oedema immediately after injection can be pronounced, but mid- or long-term oedema is very rare. This results in a high degree of predictability and precision for volumising ▷

> “Lumps, besides cases of infection or granuloma, can originate from the irregular deposition of filler, water absorption by the filler, reactive oedema or tissue response with cellular components, with or without capsule formation.”

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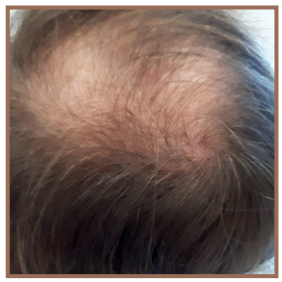

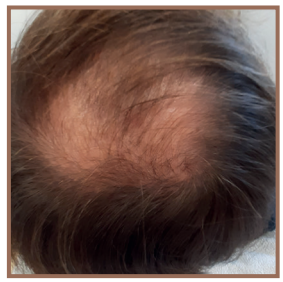

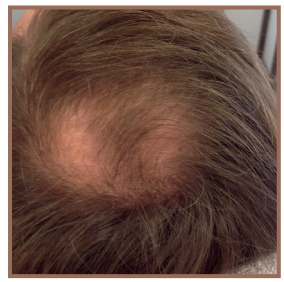

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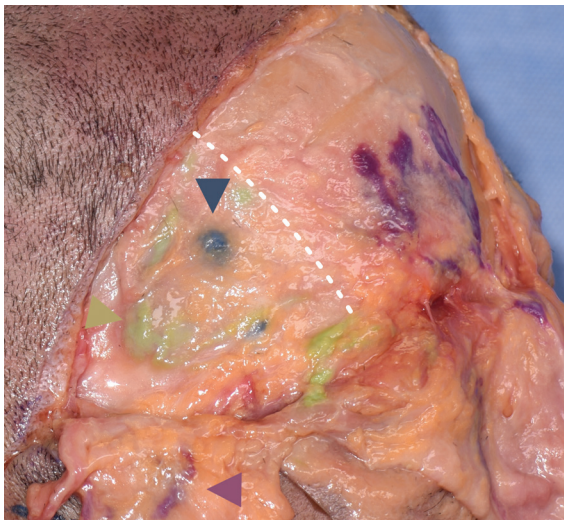

Figure 4 Cadaver dissection of the right temple after injection of dyed agarose 3.5% (Algeness DF) (blue) in the temporal muscle with a sharp 27G needle after making bone contact, 2.5% (green) deep subcutaneous (under the superficial fascia) with a cannula 25 and 1.5% (purple) subdermal with a cannula 25. The dotted line indicates the position of the temporal crest. The superficial subcutis containing the 1.5% (purple) has been dissected off the superficial fascia. Not only do we see the green 2.5% filler shining through the superficial fascia. The blue 3.5 % filler injected deep in the temporal muscle has travelled along the trajectory and some is in a deep subcutaneous position.

▷ injections (*Figure 7*). Taking the absence of any chemical modification and the complete biodegradation into account, agarose is a good option for large volume treatments (*Figure 8*).

Patient selection and counselling

The effects of facial volume correction can be less obvious than wrinkle filling or muscle modulation. Not long after treatment, patients can genuinely believe that all the fat[4] or all the filler[20] is gone, while the clinical photography evidently shows the opposite.

In cases when pigmentation problems, wrinkles, muscle hypertonia or hypercontraction are significant, treating the obvious first may inspire more patient confidence than imposing a 'from-the-basement-to-the-roof' philosophy.

What patients see in the mirror can bother them to a larger degree than how others see them from all angles. We are getting disproportionate requests about tear troughs, the nose or the lips while lateral components of a balanced strategy may be refused. Patients not being bothered by their cheekbones is a poor reason for subcutaneous injection medial to a nasolabial fold. Excessive anterior fullness can point the patient out as having been injected, and the risk of intravascular injection is higher.

> "As biostimulatory agents depend on tissue response, 3 to 4-month pictures are a fairer representation of the result than what is seen immediately or only a few days after injection."

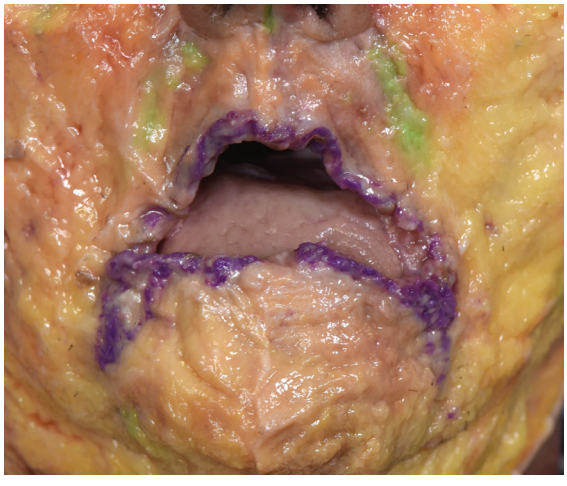

Figure 5 Cadaver dissection after subcutaneous injection of dyed agarose 2.5% (green) medial to the nasolabial folds and 1.5% (purple) in the lips. All injections were performed retrogradely with a 25G cannula. In the lips, one injection trajectory ran along the border and a second one was centred under the dry vermillion. In the central part of the upper lip, on the slightly everted right side, the two deposits are distinctly visible. The tissues on the left side were firmly remodelled by pinching and rolling immediately after injection. The deposits on the remodelled side do not appear any different than on the unremodeled side.

The high price of full-face volumising injections can take patient dissatisfaction to a different level than after wrinkle treatment.

Therefore, proper informed consent about volumising injections requires considerable time and dedication. Injecting the temples, the eyebrows, the midface and the jawline with physiological saline solution (or a low concentration of local anaesthetic[6]) on one side is a great way to show a patient what can be achieved. This is not recommended for the forehead, the orbital margins, the nose or the lips.

Typical small versus large volume treatments and levels of injection

Treatments on the orbital margin, of the nose, the lips or the chin (*Figure 9*) rarely require more than 1 to 1.4 ml. If more volume is needed, it can be wise, before injecting more, to evaluate the result after three weeks, when all swelling caused by the trauma of injecting is gone and asymmetries and imperfections of the first treatment are more apparent.

It is not uncommon for tens of millilitres of fat to be used in global facial rejuvenation by lipofilling. Although a part of the volume of injected fat disappears, one can still not expect to match the effect of global facial lipofilling by injecting only a few syringes of fillers. It is laudable that the maximal effects of minimal quantities are shown during clinical demonstrations. Nevertheless, immediate results are the sum of the injected volume and the swelling caused by the trauma of injection and remodelling. This 'workshop effect' may lead to overestimation of what can be achieved with a little quantity of filler.

Imperfections, such as hardening or irregular results, are better hidden after injection close to bone. Subcutaneous injections tend to give more visible results for less quantity. In most areas, injection close to bone holds less risk for intravascular injection than subcutaneous administration, while the latter, unjustly, may look less frightening to the inexperienced injector. Deep injections may be better at compensating lack of bony support. Extra superficial volume adds weight, which may pose a problem in descending soft tissue, e.g. close to the jowls. However, a subdermal injection may offer other benefits than volume augmentation. The gentle biostimulatory effect of calcium hydroxyapatite can improve skin firmness.

More therapeutic modalities for tightening and lifting have become available. Subdermal induction of heat, focused ultrasound, and suspension sutures require passage through the superficial compartments or target the superficial musculoaponeurotic system (SMAS). As we have very little data on interactions, it is wise to limit filler injections to deep and, for wrinkle filling, strictly intradermal if other subcutaneous treatments have been performed or are considered (*Figure 10*).

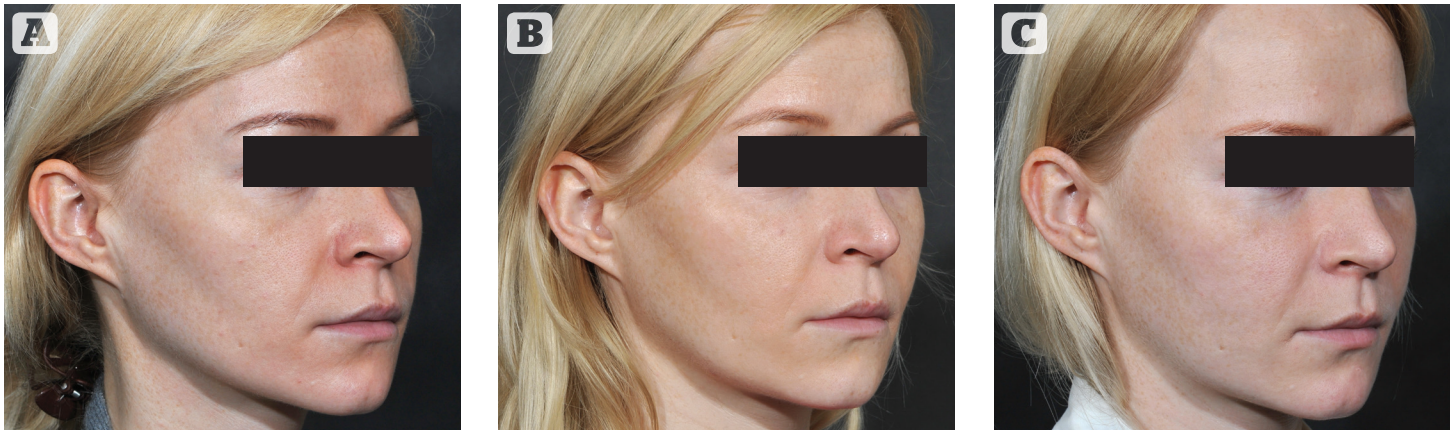

Figure 6 This 28-year-old lady was treated by injection of 2 ml of HA (Belotero volume) on each side, close to bone on the zygomatic body and arch (also some on the adjacent parotid fascia) and on the lateral aspect of the maxilla. (A) Situation before injection. (B) After three months, increased malar mound projection, better blending with the cheek hollow and the anterior cheek, and a decreased tear trough hollow (without direct injection) are obvious. (C) After a year, the projection of the malar eminence appears less prominent, more by inflation of tissues surrounding it than by true loss of volume in situ. The positive effect on the tear trough hollow and much of the overall aesthetic improvement persist.

Variability of results and mid- to long-term oedema

As biostimulatory agents depend on tissue response, 3 to 4-month pictures are a fairer representation of the result than what is seen immediately or only a few days after injection. If the result of a small treatment looks pleasing in the mid-term, the use of larger quantities in that individual is more justified.

The low cellular response to HA fillers makes them more versatile for all levels of depth in facial rejuvenation. Soft lumps can be remodelled to some extent, while cellular aggregates or capsules cannot. The downside of HA is that the degree of reactive focal, local and locoregional oedema is hard to predict. Signs and symptoms of facial oedema, such as malar mounds or variable size of baggy eyelids throughout the day, and previous reactive swelling after HA injection, are relative contraindications, at least in and around the affected areas.

A little oedema may not be taken as a disadvantage by patients with relatively tight skin or those who revel in a slightly exaggerated lip profile. They may appreciate it as more result per volume. Nevertheless, injection of the lips, on the inferior orbital margin or superficially in the temples and the use of large quantities, in general, hold the risk of an oedematous, overinflated and unnatural look in some patients, especially those with lax soft tissues and thin skin. It is highly recommended to divide large volume HA treatments into multiple sessions, with intervals of at least three weeks. Clinical photography at 3 months and later is very helpful in detecting light puffiness and allowing the practitioner to act or abstain from action accordingly.

Agarose allows us to modify a face in a predictable manner with the injected volume and only that. Experienced patients need to be advised that no reactive oedema also means no more volume than the quantity injected. Great care has to be taken to avoid the formation of visible or palpable nodules when concentrations that are too high are deposited in contact with the dermis.

Due diligence in education

Sound knowledge of the anatomy, of aesthetic principles including age-, gender-, ethnicity- and culture-related changes, of injection techniques and safety are a prerequisite for volumising injections.

While intradermal injections in the vicinity of pore and adnexal microbiomes appear to be more forgiving, acute and low-grade subcutaneous or deep infections can have catastrophic consequences. After proper cleaning and preparing of the skin, maintaining the sterility of cannulas, needles and products cannot be forgone. Window-dressing with sterile drapes around a field that includes unprepared zones, or with sterile gloves for handling non-sterile equipment is not helpful.

It is easiest to reach anatomical points precisely with ▷

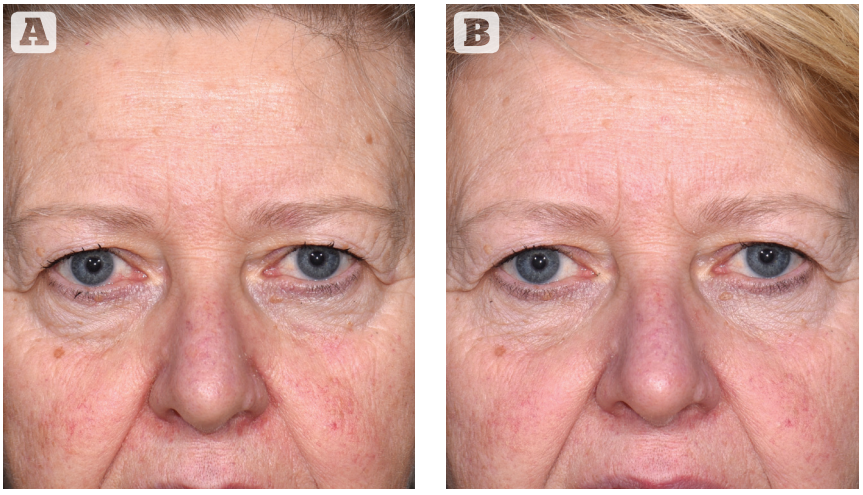

Figure 3 This 62-year-old lady requested a minimally invasive treatment of the orbital margins, insisting that she accepted her signs of ageing except for the 'tired look'. The thin skin and protruding orbital fat in the lower eyelids pose a high risk of reactive oedema and irregularities after HA injection. (A) Situation before the treatment. (B) Result three months after the injection of agarose 1% under the orbicularis oculi muscle with a 27G cannula, 0.7 ml on each side. For security reasons, the author currently advocates the use of a 25G cannula unless, at the end of the treatment, a remaining depression can only be reached with a thinner cannula.

Figure 8 This 27-year-old lady, who has a retruded central midface, was treated with 33.6 ml of agarose 1%, 1.5%, 2.5% and 3.5% in 10 sessions at intervals between 3 weeks and 3½ months. She was injected close to bone on the orbital margins, anteriorly on the maxilla, including the premaxilla and the zygomas. The mentioned quantity also includes intercrural and dorsal nasal injections and lip augmentation. The nasolabial wrinkles were injected intradermally with 1 ml of HA (Belotero Intense) at two occasions during the same period. (A) Situation before the treatment. (B) Result 1 year and 8 months after the first and 2 months after the last treatment.

▷ sharp needles. They cause less pain than cannulas when penetrating thick muscles (temporal, masseter, depressor labii inferioris). Cannulas make it easier to follow anatomical planes, such as between the superficial and muscle temporal fascia or under the orbicularis oculi muscles. If their calibre is 25 G or larger, their safety profile is better[21]. Because severe complications are rare, statistical evidence for preventive measures is hard to find, if at all. Nevertheless, knowledge of the different safety profiles of the fillers, the tools to inject them, and the preventive measures mentioned earlier[11], help us to base injection techniques on reason rather than on intuitive preference.

Figure 9 This 28-year-old lady was injected with 1 ml of HA (Belotero Volume) close to bone on the chin with a 30 G needle in small aliquots no larger than 0.1 ml. (A) Situation before the treatment. (B) Result after 5 months. Improving chin projection in patients with a small degree of retrognathism or retrogenia can contribute significantly to overall facial harmony, while the required quantity of product is relatively small. Because of increased support, the mentalis muscles have to contribute less to mouth closure. The skin dimpling on this patient's chin disappeared after the treatment.

Academic training programmes are evolving, but much of the knowledge about volumising injections is gathered at congress lectures and demonstrations. We would not stand where we are without training and workshops organised by the industry. More and more detailed descriptions of injection techniques[18,20,22] are appearing in peer-reviewed literature. No single product can cater to all needs and practitioners are recommended to build knowledge across brands and companies and make their choices independently.

Cadaver courses offer great opportunities to improve knowledge about anatomy. Seeing the structures that we inject helps to understand the effects of our actions in clinical practice, although the vascular detail as exposed by a professional anatomist after the injection of intra-arterial resin will not be found. While we hope to work at precise levels and follow anatomical planes, it can be humbling to discover to what extent filler is deposited in adjacent structures (*Figure 3*).

Observational learning is different from personally injecting and dissecting. For proper dissection, tedious tasks have to be taken at heart. Raising the skin at the immediate, subdermal level or raising superficial fat flaps following anatomical planes can take a lot of time before any proper results can be seen. Deep, exploratory incisions without sufficient exposure lead to flipping tissue back and forth, thereby squeezing oil from the fat compartments, to messing up the dissection field, and frustration.

> "It is easiest to reach anatomical points precisely with sharp needles. They cause less pain than cannulas when penetrating thick muscles (temporal, masseter, depressor labii inferioris)."

For supervised injection and dissection of all injectable areas of a face by two participants, alternating with lectures about the anatomy and clinical applications, at least two days are required, three are better. It may help to clearly differentiate in course programmes between observation and the opportunity to completely dissect the result of one's own injections, including the effort it takes.

Clinical observation and hands-on training are particularly important to develop practical skills. It is helpful for trainers to grade anatomical targets by difficulty and risk. Deep needle injection of the temples or the chin are not difficult and carry less risk of intravascular injection. Cannula injection of the retro orbicularis oculi fat pad (ROOF) under the tail of the eyebrow, or of the nasolabial subcutis, is not difficult but carries a relatively high risk of catastrophe in case of intra-arterial injection. Orbital margin, nose and lip injections are difficult and carry a higher risk.

Furthermore, protection of retinal circulation by external compression of collaterals can be arranged for nasal or ROOF treatment, not for A-frame or inferior orbital margin enhancements.

Research and development

Magnetic resonance imaging is becoming less expensive and calculating volume change from 3D photography more refined. Quantified evidence about mid- and long-term results would offer more than immediate results in demonstrations, selected clinical photography and patient satisfaction scores.

Remarkably few histologic reports have been published about filler behaviour and tissue response outside the scope of intradermal injections or filler complications. As muscles, fat compartments and connective tissue are being injected, such data would be welcome.

Automated injection devices, delivering precise micro-boluses or gentle, continuous flow, with a safety stop triggered by high-pressure gradients, are already at hand[23,24]. They can prevent us from exerting too much pressure to unblock a clogged-up needle, or from injecting too fast after a pressure drop on entering a blood vessel. It would greatly contribute to safety if every injection could be preceded by automated aspiration.

The smaller the calibre of a needle, the smaller the bolus that can be injected over a given amount of time, even under relatively high pressure. This may help to reduce the consequences of inadvertent intravascular injection. The evolution towards volumising fillers that can pass a 30G needle has been a step forward for safety and remains a good standard for new developments.

The only terminal arteries in the face are the central retinal arteries. The only clinically documented compartment syndrome in the face is a retrobulbar hematoma. For injections to cause necrosis in any other area of the face, external pressure or segmental embolisation of an artery is (fortunately) insufficient. The block has to extend into the capillaries because collateral arteries otherwise maintain perfusion. How progressive, intravascular coagulation and inflammation contribute to the ischemia deserves further attention. Skin appearance after embolisation does not necessarily go from pallor to livedo reticularis[9] as described by DeLorenzi. Clinical pictures on HA embolisation cases show bright red zones containing small foci of necrosis[25,26]. Both the redness and gradual progression into adjacent zones[26] are indications of an expanding inflammatory process, leading to focal, intravascular coagulation. Laboratory studies comparing what happens after intravascular injection of different fillers would be most welcome.

Conclusions

Over the last decades, we have witnessed a multiplication of anatomical knowledge relevant to volumising treatments. A large array of injectables are now available, including volumising fillers, biostimulants, and combinations. Indications are growing in numbers. ▷

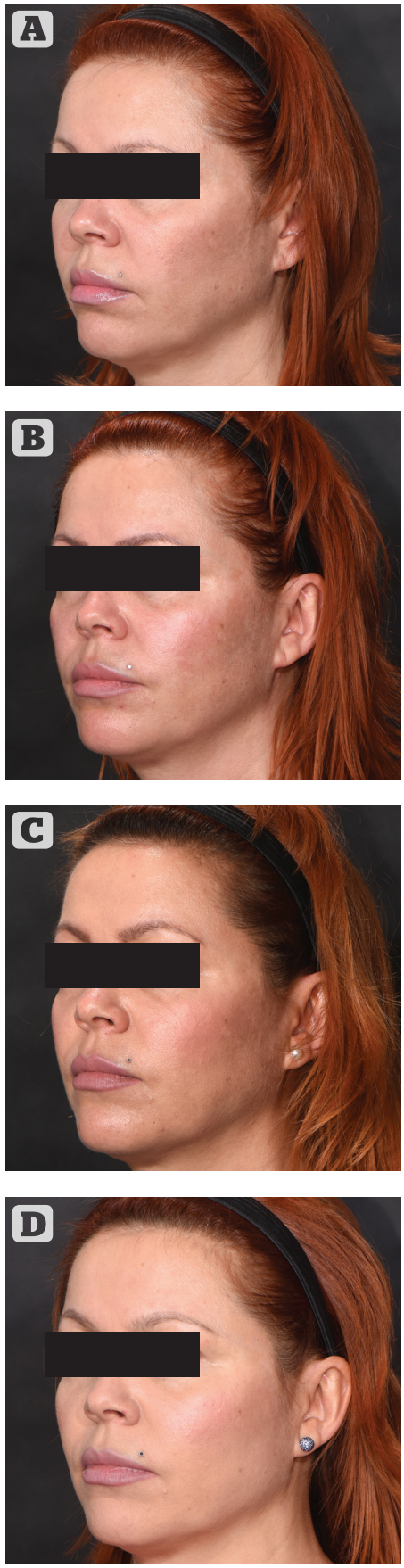

Figure 10 This 42-year old lady was treated with agarose injections and by subdermal induction of heat (Attiva******) (A) Situation before treatment. There is light descent of the eyebrows and the soft tissues of the lateral midface and lower third. There is lack of chin projection. (B) result five weeks after deep chin injection with 1.4 ml of agarose 2 %. (C) Result three months after subsequent subdermal induction of heat. Please note the elevation of the eyebrows and the soft tissues of midface and over the jawline. (D) Result two months after the last of two subsequent injection sessions with a time interval of one week. A total of 5.6 ml of agarose 2.5% and 3.5% was injected close to bone in the lateral midface and on the mandibular angle, and 0.7 ml of agarose 1% was used on each inferior orbital margin. Full faces can sometimes be made more elegant by increasing the projection of selected points. These pictures were shown at the IMCAS conference in Paris on 3 February 2018 during the presentation: 'Contraction plus expansion: facial soft tissue tightening combined with deep agarose injections'.

> "For supervised injection and dissection of all injectable areas of a face by two participants, alternating with lectures about the anatomy and clinical applications, at least two days are required, three are better."

Key points

- The biostimulatory effect of volumising fillers varies from minimal (hyaluronic acid), mild (agarose), intermediate (calciumhydroxylapatite) to strong (polylactic acid)
- HA lumps are only slightly difficult to manage, hard lumps may occur with other fillers
- Uncross-linked agarose disperses in water, also intravascularly. HA's, calciumhydroxylapatite and polylactic acid do not. HA can be dissolved completely, the other fillers cannot
- The biostimulation by calciumhydroxylapatite and polylactic acid is variable. HA's absorb water, at times induce oedema and blur contours. Agarose is 'what you see is what you get' or WYSIWYG
- High definition volume photographic scanning is not available for the face and MRI is still too expensive. Histology and biomechanics of injected tissues and embolization mechanisms demand further investigation
- Expertise demands advanced training in the anatomy lab and hands-on training

▷ Reasonably extensive information has been published about tolerance, safety, patient satisfaction and rare but severe complications. Histology of filler behaviour and tissue response is scarce, as are quantified data about volume increase per unit of injectable and resorption over time.

Volumising treatments are of three-dimensional complexity without the control of surgical exposure. Obtaining informed consent requires more time and effort than for muscle modulation and wrinkle filling. Peer-reviewed literature on injection techniques, hands-on training and cadaver courses help to progress from basic treatments to complex injections and those with more inherent risk of serious adverse events.

> **"A large array of injectables are now available, including volumising fillers, biostimulants, and combinations. Indications are growing in numbers."**

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▶ *Dr. Vandeputte is a consultant and trainer for Merz Pharma Merz Pharma GmbH & Co. KGaA, Frankfurt am Main, Germany and for Advanced Aesthetic Technologies Inc, Brookline MA, USA (AAT).*

▶ *The dissections show in this article were performed at the Cadaveric Microanatomy Centre, Applied Science University, Amman, Jordan and were funded by AAT, as part of the Algeness Inject and Dissect Course, 27-29 August, 2019, chaired by the author.*

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