

Polynucleotides Highly Purified Technology and the face skin, a history of innovative skin priming

Alberto Massirone

Founder of the Post-graduate School of Aesthetic Medicine (SMIEM)
President of Agorà, Italian Scientific Society of Aesthetic Medicine, Milan

Received for publication November 16, 2020; accepted March 25, 2021 - © Salus Internazionale ECM srl - Provider ECM no 763

Corresponding Author

Alberto Massirone, MD

Founder of the Post-graduate School of Aesthetic Medicine (SMIEM)
President of Agorà, Italian Scientific Society of Aesthetic Medicine, Milan

E-mail: mail@albertomassirone.com

Skin tonicity and roughness control are especially crucial in the perioral, periocular, and cheeks and eyelid areas as well as the décolleté, including the neck. Crow's feet and generally all wrinkling of facial senescent skin is almost entirely the result of dermal changes, associated with the depletion and fragmentation of elastin and collagen fibres and increasing scarcity of fibroblasts¹.

Many aesthetic medicine treatments may enhance the appearance of face skin without general anaesthesia and surgery. Some examples are chemical peeling, fillers, skin boosters, botox injections, radiofrequency, laser, and microdermabrasion treatments. The preliminary study of the patient's skin and personalized treatment protocols based on a combination of different procedures allow for the best rejuvenation outcomes. Today it might be reasonable to consider highly purified, natural-origin polynucleotides (PN-HPT™, Polynucleotide Highly Purified Technology) as the critical foundation of a wealth of aesthetic treatments.

PN-HPT™ improve dermal trophism and overall skin turgidity; moreover, acting as re-activating "primers" of dermal tissues, PN-HPT™ can improve the outcomes of other skin rejuvenation techniques. PN-HPT™ are indeed extensively used to prime the skin before aesthetic treatments with fillers and polydioxanone thread lifts; PN-HPT™ may also be important before radiofrequency and laser treatments because better aesthetic results are achieved in hydrated and metabolically active tissues^{1,2}. Products containing long-chain, highly concentrated polynucleotides of high molecular weight combine the filling efficacy of conventional linear HA-based products with powerful regenerating efficacy on the dehydrated wrinkles of sagging and aging face skin².

Several Class III CE 0373 PN-HPT™-based medical devices for intradermal infiltration are commercially available in Italy, Europe and on extra-European markets, as single-agent formulations^(a) or co-formulated with hyaluronic acid^(b), for the face, neck, décolleté, and other critical face areas such as perioral and periocular skin, the cheeks and eyelids.

As extensively described in this narrative review, with special reference to the previous "Introduction to Polynucleotides Highly Purified Technology"

section, intradermally infiltrated PN-HPT™ increase skin turgidity, hydration and elasticity by promoting the activity of dermal fibroblasts and the *de novo* regeneration of autologous glycosaminoglycans, fibril proteins, and glycoproteins (Figure 1).

PN-HPT™ may be of especially great benefit to areas like the neck and the décolleté, where the aesthetic medicine specialist does not have many alternatives and skin ageing is often more severe than in face skin.

As regards periocular skin and eyelids, both aesthetically sensitive areas due to locally thin skin, PN-HPT™ may once again act as re-activating "primers" of dermal tissues before and in concomitance with other treatments.

Thanks to such "priming", specifically formulated PN-HPT™ formulations may enhance tissue tightening and improve the efficacy of other widely used skin tightening and rejuvenating techniques widely used in these areas, like botox infiltrations or laser and plasma treatments. Low-concentration PN-HPT™ formulations have the additional benefit of avoiding the subjectively unpleasant persistence of wheals for some hours, as may happen with more concentrated PN-HPT™ formulations with or without HA¹⁻⁴.

(a) Plinest® (PN-HPT™ intradermic gel, 20 mg/mL, 2 mL pre-filled syringes), Plinest® fast (PN-HPT™, 7.5 mg/mL, 2 mL pre-filled syringes), Plinest® Eye (PN-HPT™ for eye contour, 2 mL pre-filled syringes) - Mastelli Srl, Sanremo (Italy)

(b) Newest® (PN-HPT™ and HA, both at a concentration of 10 mg/mL, and mannitol 200 mM per liter, 2 mL pre-filled syringes) - Mastelli Srl, Sanremo (Italy)

The prolonged isosmotic hydration of the dermal matrix contributes to preserve the ideal conditions for fibroblast metabolic activation over time in face skin^{6,8,9}. The text box outlines two representative examples of available clinical findings that illustrate the boosting power of PN-HPT™ on face skin.

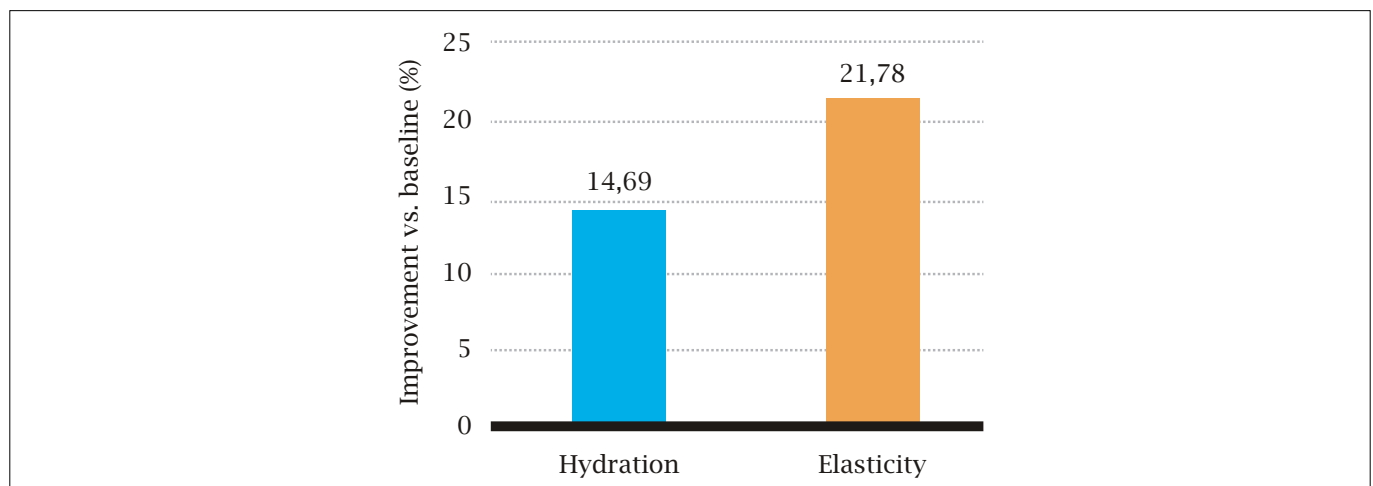


Figure 1 - Skin hydration and elasticity: percent improvement after intradermal infiltration of PN-HPT™ in 143 subjects of both sexes (Plinest®, Mastelli Srl, Sanremo; serial or micro wheals technique, retrograde linear injections or cross-link technique), 3-4 sessions every 1 to 2 weeks, evaluation one month after the last infiltration⁷.

■ Overall clinical improvements due to orthodermis and reductions of superficial fine wrinkles (*Figure 2a*) can be expected in more than 90% of individuals after PN- HPT™ intradermal infiltrations (40 mg/2 mL, 30G-needle Plinest® pre-filled syringes; 3 or 4 infiltration sessions according to the type of skin). The evidence is not only subjective in treated subjects, but it is also objectively supported by the quantitative outcomes of analyses with the camera-associated ANTERA® 3D CS skin imaging devices (*Figure 2b*)⁵. As shown in a two-year study in 148 patients of both sexes (134 females and 14 males), with ages ranging from 32 to 75 years, the increase in face skin turgidity in the days immediately following infiltration is associated with readily appreciable skin texture improvements. The best clinical results are appreciated after about one month after the last treatment (91% of “improved” global assessment by the Investigator, along with a 21.8% increase in hydration and improved elasticity

(*Figure 3*)¹. Thin periocular skin is an area where PN-HPT™ appear to offer distinctive aesthetic outcomes with a specific 15 mg in 2 mL protocol (e.g., Plinest® Eye, Mastelli Srl)^{6,7}. *Figure 4* illustrates a study based on such a protocol (micro-wheal technique). Tightening of the periocular skin translated into the disappearance of the most severely sagging areas⁶.

■ If the aesthetic choice falls on a PN-HPT™ + hyaluronic combination (e.g., Newest®, Mastelli Srl), the infiltration technique may leverage the benefits of handy, thin and flexible cannulas (diameter 27 G, length 37 mm) which minimize problems associated with standard needles (e.g., diameter 30 G, length 13 mm-discomfort, bruises, especially in the periocular and perilabial areas, the need to repeatedly reposition the needle to treat extensive skin areas, slower recovery, less uniform technique⁷.

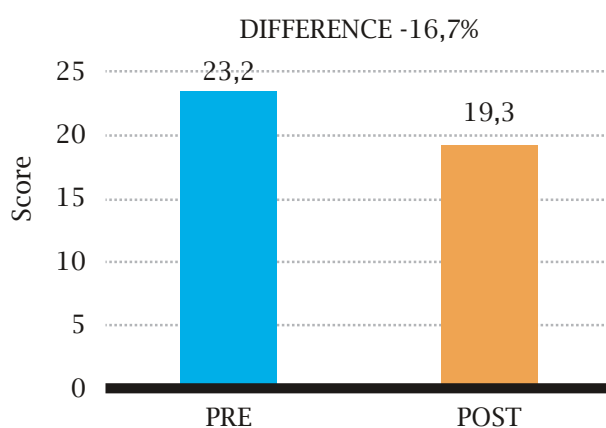


Figure 2a - Roughness (%) of less than 2.5 mm in the lateral dimension: baseline (PRE) and after 30 days of follow-up with 3 to 4 PN-HPT™ (Plinest®) infiltration sessions (POST)⁵.

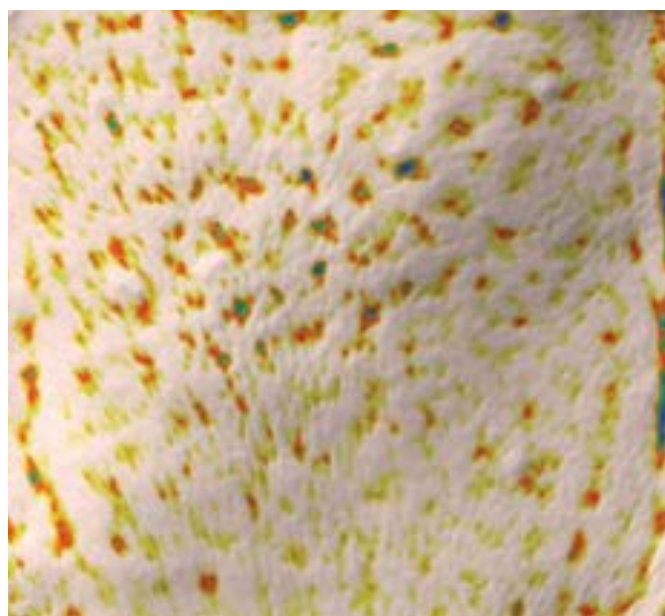
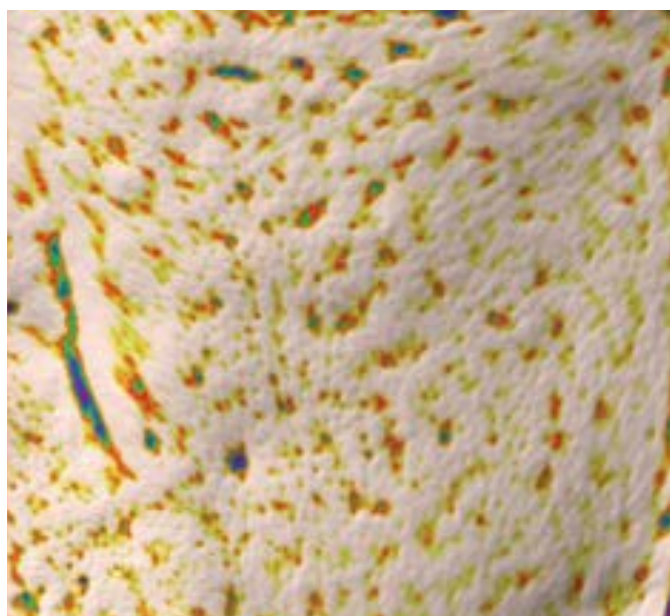


Figure 2b - Objective improvement of skin texture in the treated face area (camera-associated ANTERA® 3D CS skin imaging device): baseline (left) and after 30 days of follow-up with 3-4 PN-HPT™ (Plinest®) infiltration sessions (right)⁵.



Figure 3 - Left: before neck treatment with long-chain PN-HPT™ (Plinest®, Mastelli Srl), right: one month after four PN-HPT™ sessions: reduction of fine wrinkles and improvement of tonicity and overall skin appearance¹.

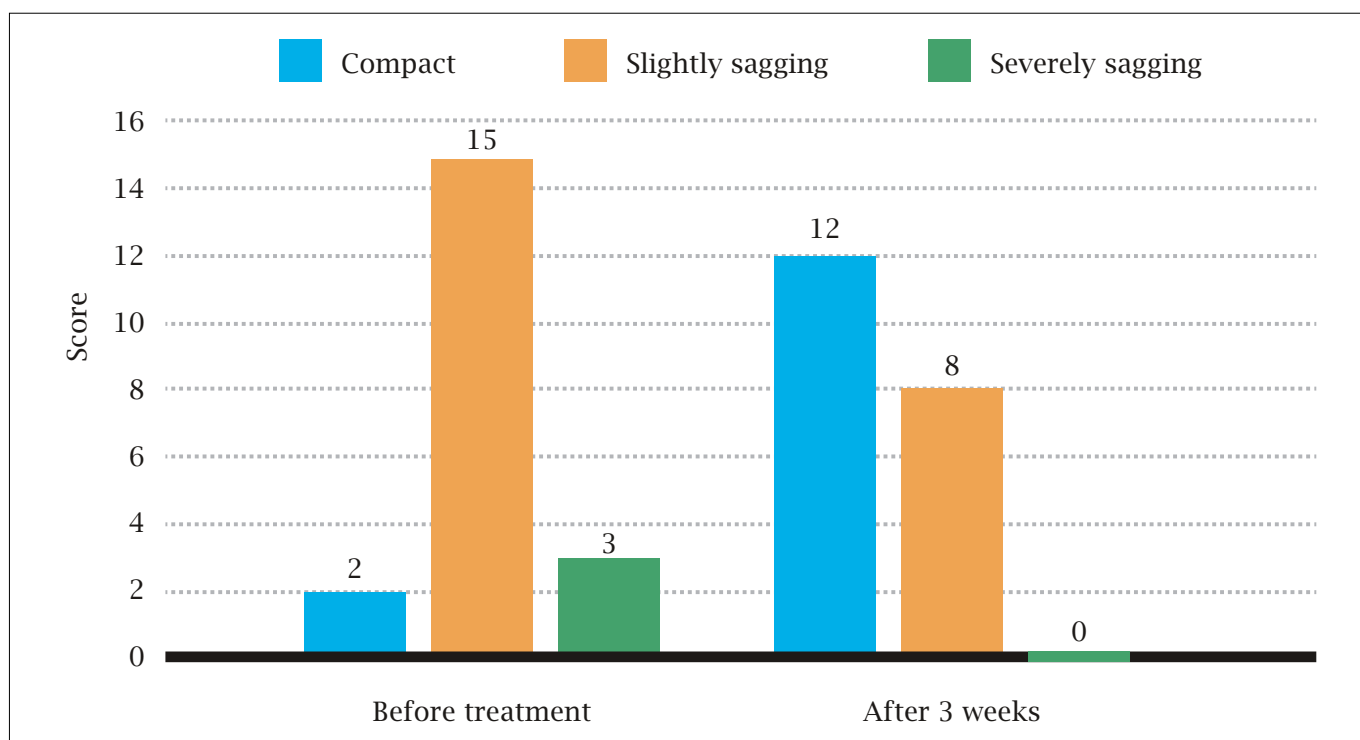


Figure 4 - Quality of the periocular skin texture after 3-4 sessions of treatment with Plinest® Eye (Mastelli Srl): outcomes after one month (absolute count of favourable aesthetic self-assessment by 20 subjects)².

Suggested PN-HPT™ infiltration technique in face skin biorevitalization

Based on clinical experiences, a standard treatment protocol for skin face biorevitalization could be as herein described, associated with the at-home application of PN-HPT™-based creams/gels/food supplements, as strongly advised. As always (for comparison see also the “Introduction to Polynucleotides Highly Purified Technology” section), the first period of PN-HPT™ infiltrations (micro-wheal technique, either with a linear or reticular distribution of intradermal infiltrations) could be followed either by further PN-HPT™

infiltrations without concomitant hyaluronic acid or by combined PN-HPT™ + hyaluronic acid infiltrations, in agreement with the “PN-HPT™ priming” strategy. Intradermal infiltrations should be performed with very thin needles (30 G). The following techniques are advised: micro-wheal technique spaced 0.5-1 cm or retrograde linear infiltrations (ideal for filling superficial and/or medium dermis wrinkles, Langer lines or in large skin areas such as cheeks or nasolabial folds) or cross-link (reticular) technique (net of linear intersecting infiltrations, ideal for widely distributing PN-HPT™ over large skin areas, such as the cheeks). The infiltration technique may leverage the benefits of thin

flexible cannulas (diameter 27 G, length 37 mm) that minimize the problems of standard needles-discomfort, bruises (with special reference to the periocular and perilabial areas), repeated needle repositioning to treat extensive skin areas, slow recovery, and less uniform technique⁷.

Neck and décolleté biorevitalization - PN-HPT™ or PN-HPT™ + HA, one session every 2-3 weeks for a total of 3-4 infiltrations. Maintenance long-term treatment: repeat at-home treatment with a PN-HPT™-based gel every 1-3 months, strongly advised.

Eyelid biorevitalization - PN-HPT™ in specific formulations for thin, sensitive areas like Plinest® *fast* (15 mg in 2 mL), 1 session every week or every two weeks for a total of 3-4 infiltrations. Maintenance long-term treatment: repeat every 1 to 3 months. At-home periocular treatment with a nucleotides-based gel is strongly advised.

Face and perioral biorevitalization - PN-HPT™ (40 mg in 2 mL) or PN-HPT™+HA (20 mg + 20 mg in 2ml): one session every 2-3 weeks for 3-4 infiltrations. Maintenance long-term treatment: PN-HPT™ or PN-HPT™ + hyaluronic acid infiltrations every one or two months. At-home PN-HPT™- based gels/creams/food supplement are strongly advised.

REFERENCES

1. Cavallini M, Papagni M. Long chain polynucleotides gel and skin biorevitalization. *J Plast Dermatol.* 2007; 3(3):27-32.
2. Cavallini M. Biorevitalization and cosmetic surgery of the face: synergies of action. *J Appl Cosmetol.* 2004; 22(3):125-32.
3. Guizzardi S, Uggeri J, Belletti S, Cattarini G. Hyaluronate increases polynucleotides effect on human cultured fibroblasts. *J Cosm Dermatol Sci Applic.* 2013; 3(1):124-8.
4. Landau M, Fagien S. Science of hyaluronic acid beyond filling: fibroblasts and their response to the extracellular matrix. *Plast Reconstr Surg.* 2015; 136(5 Suppl):188S-195S.
5. Cavallini M, Cattarini G, Papagni M. High technology skin biorevitalization with polynucleotides: clinical experience in anti aging treatments. Poster presented at the Anti-Aging Medicine World Congress (AMWC) 2014, 12th edition, Monte Carlo (Principality of Monaco).
6. Cavallini M, Papagni M. Trattamento integrato del contorno occhi. *L'Ambulatorio Medico.* 2013; 39:11-2.
7. Ulgiati S, Pompilio L, Santini S. Polinucleotidi e acido ialuronico: ago tradizionale o cannula? *L'Ambulatorio Medico.* 2018; 53:11-13.
8. Park KY, Seok J, Rho NK, Kim BJ, Kim MN. Long-chain polynucleotide filler for skin rejuvenation: efficacy and complications in five patients. *Dermatol Ther.* 2016; 29(1):37-40.
9. Pak CS, Lee J, Lee H, et al. A phase III, randomized, double-blind, matched-pairs, active-controlled clinical trial and preclinical animal study to compare the durability, efficacy and safety between polynucleotide filler and hyaluronic acid filler in the correction of crow's feet: a new concept of regenerative filler. *J Korean Med Sci.* 2014; 29 Suppl 3:S201-9.