**REFERENCES**


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**TEOSYAL® PureSense**

**Deep Lines**

In-depth filling

- HA 25 mg/g
- Volume-creating capability: 6666
- Indications: Filling deep wrinkles
- Injection area: Deep dermis
- Blister pack: 2 x 1 ml
- Estimated duration*: 9 months on average

**Ultra Deep**

The gentle way to give volume

- HA 25 mg/g
- Volume-creating capability: 6666
- Indications: Very deep wrinkles in thick skin
  Creates and restores volumes, facial contours
- Injection area: Hypodermis
- Blister pack: 2 x 1 ml - 2 x 1.2 ml
- Estimated duration*: 12 months on average

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*Average duration depends on several factors: patient's skin type, severity of the wrinkle to be corrected, type of injection (superficial, medium or deep dermis) and the volume injected.

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OBJECTIVE
This study assesses by 2 methods the mechanical performances of hyaluronic acid (HA) based injectable fillers: one, commonly used, measures elastic (or storage) modulus G' and the other measures the flattening resistance of the gel, i.e. its cohesivity.

INTRODUCTION
Most of fillers are based on crosslinked HA. Crosslinking allows to interconnect HA chains by creating bonds between them. Although only a minor part of the HA chain is modified (usually less than 10%), this transformation considerably increases the biomechanical properties of the material and its resistance to enzymatic and free radical breakdown. As the fillers’ efficacy is mostly related to their mechanical properties, several studies aimed to classify products according to rheological measurements, and usually by using a single essential parameter as the elastic modulus G' or complex modulus G*. [1-5]

Nevertheless, by combining 2 experimental protocols and measurements, the Lift Capabilities concept[6] offers a much more reliable view of the effective mechanical capabilities of a filler:

- Elastic modulus G' characterizes the solid-like contribution to the measured stress response and quantifies the gel “hardness” at rest [Protocol 1: dynamic oscillatory test].
- Cohesivity is used to assess the filler ability to resist to deformation and to destructuring [Protocol 2: compression test].

These 2 protocols consider different types of mechanical stresses applied to the fillers. The results shown below were obtained by studying 6 commercially available dermal fillers.

MATERIAL AND METHODS
The fillers were obtained from commercial sources. A same batch of each product was tested before expiry date, the references of batches are given in Table 1, (before expiry date).

Rheology : Dynamic oscillatory test
Tests are performed at 25°C and Hi frequency, with amplitude sweep corresponding to an applied deformation strain from 1 to 1400 Pa, using a Thermo Haake RS3000 rheometer with a 35mm / 1° Titane cone-plate geometry. The resulting stress response is measured: G' is recorded at low strain (r < 5 Pa), i.e. almost at rest.

Compression test
2.5 g of gel are placed between the 2 plates of a 35mm / 1° Titane cone-plate rheometer. The rheometer is set to a Normal Force mode: the upper plate is put in contact with the gel and is lowered toward the bottom plate, thus compressing the gel. The course is stopped when 70% of compression is reached. The resulting normal force is measured during the experiment, from 0 to 70% compression rate.

RESULTS AND DISCUSSION
Figures 1 and 2 show the results obtained with oscillatory rheology and compression test.

Figure 1: Elastic modulus G’ as a function of the strain applied

Generally, G’ values are recorded at small-deformation (r < 5 Pa), where G’ remains constant (viscoelastic region). The values obtained here (table 1) are in accordance with the literature, taking into account small differences between experimental protocols. [1-2, 4] After a threshold called critical strain, the gel disrupts its structure and G’ drops (yield stress). The critical strain occurs earlier or later depending on the gel tested. The greater the critical strain, the more stable is the gel structure. Restylane® and Perlane® show weak critical strain.

Figure 2: Forces resulting from the compression of the gel, as a function of the compression rate

Figure 2 shows, for different fillers, the force required in order to flatten the gel with a linear increasing degree of compression from 0 to 70%. The curves allow to distinguish 2 types of materials:

1- THE LOW-COHESIVITY GELS: such as Restylane® and Perlane®, for which the compression force is weak and increases to a very low extend with the compression degree (flat profile). The main part of the energy applied to the system is dissipated by the gel destructuration. The structure of the gel is weak and it does not behave as a spring.

2- THE HIGH-COHESIVITY GELS: such as Teosyal® and Juvéderm®, for which the compression force increases strongly. These gels behave like a compressed spring, the main part of the energy applied can be returned. They also have the ability to recover their shape after compression and they resist well to compression.

The calculation of the area under the curves (fig. 2) gives a cohesivity index (table 1).

G’ values and cohesivity indexes can be combined in order to assess the Lift Capabilities, as shown in the figure in the box. Teosyal® PureSense Deep Lines and Ultra Deep show high G’ because they are designed for the filling of deep wrinkles and for the creation of volume in the face. They also display the highest cohesivities. The Juvéderm Ultra 3 and 4 gels are slightly less cohesive, and have lower G’.

The cohesivities are measured by applying a pressure directly on the material. Such a mechanical stress is quite similar to the pressure sustained by the implant in vivo: in the skin, the filler is constantly submitted to compression forces caused by the muscles around. Whatever the implantation site is, it is essential that the gel has a high cohesivity in order not to disrupt its structure under the skin and to maintain a natural aesthetic result.

The gels called “particular” (as Restylane® and Perlane®) display very high G’, which drops quickly when the material is put in movement (fig. 1). Their cohesivity is also very low compared to Teosyal® PureSense Deep Lines and Ultra Deep. These features indicate a risk of non-natural aesthetic results (“hard” gels at rest) and a risk of rapid destructuration.

These observations demonstrate that compared to basic studies taking into account only G’ (elastic modulus), the study of Lift Capabilities offers a much better tool in order to assess and anticipate the mechanical properties of dermal fillers in the skin.

CONCLUSION
In order to reach an optimal dermal filling result, 2 properties are required for an HA-based gel:

- Good ability to fit to the shape of its environment, in static position as well as when the skin moves, in order to assure a natural aesthetic result.
- Elastic modulus G’, giving an indication of the gel “hardness”, should be tuned to the indications sought: filling of medium or deep wrinkles.
- Resistance to pressures and movements of the skin, in order to guarantee a good preservation of the implant structure and an extended durability of the mechanical properties.
- A high index of Cohesivity promotes a better resistance to mechanical degradation and to gel migration, and thus induces a better duration in the skin.

Teosyal® PureSense Deep Lines and Ultra Deep are intended for deep wrinkles filling and for the creation of volume in the face. These gels provide a much better tool in order to evaluate the mechanical capabilities of HA-based dermal fillers.

REFERENCES
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