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Differentiation of NASHA and OBT Hyaluronic Acid Gels According to Strength, Flexibility, and Associated Clinical Significance

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ABSTRACT

Background: With a wide range of hyaluronic acid (HA) filler products available, knowledge of gel characteristics is a key part of tailoring treatments to each patient's aesthetic goals. This paper presents 2 main gel characteristics – strength/firmness and flexibility – for HA fillers produced using NASHA® and OBT™ and their clinical significance for tissue performance.

Methods: Three NASHA gels (Restylane®; Restylane Silk; Restylane Lyft) and 4 OBT gels (Restylane Refyne; Restylane Kysse; Restylane Volyme; Restylane Defyne) were studied in dynamic mode using a PP25 rheometric measuring system at 25˚C. Gel strength/firmness was measured using frequency sweep, with G prime evaluated at 0.1 Hz. Flexibility assessments used amplitude sweep measurements between 0.1% and 10,000% strain at 1 Hz, with xStrain being the strain value at the crossover point where G prime and G double prime have the same value.

Results: Restylane, Restylane Silk, and Restylane Lyft had G primes of 701, 416, and 799 Pa, respectively. OBT G primes for Restylane Refyne, Restylane Kysse, Restylane Volyme, and Restylane Defyne were 70, 160, 171, and 271 Pa, respectively. The xStrain values were 1,442% (Restylane Refyne), 908% (Restylane Kysse), 930% (Restylane Volyme), 761% (Restylane Defyne), 7% (Restylane), 19% (Restylane Silk), and 17% (Restylane Lyft).

Conclusions: OBT products had high flexibility (tolerance to deformation) and low to intermediate strength/firmness, which make them appropriate for dynamic facial areas. NASHA products showed greater strength/firmness, with the potential to create lift and projection. Altogether, NASHA and OBT HA gels covered a wide range of strength and flexibility.

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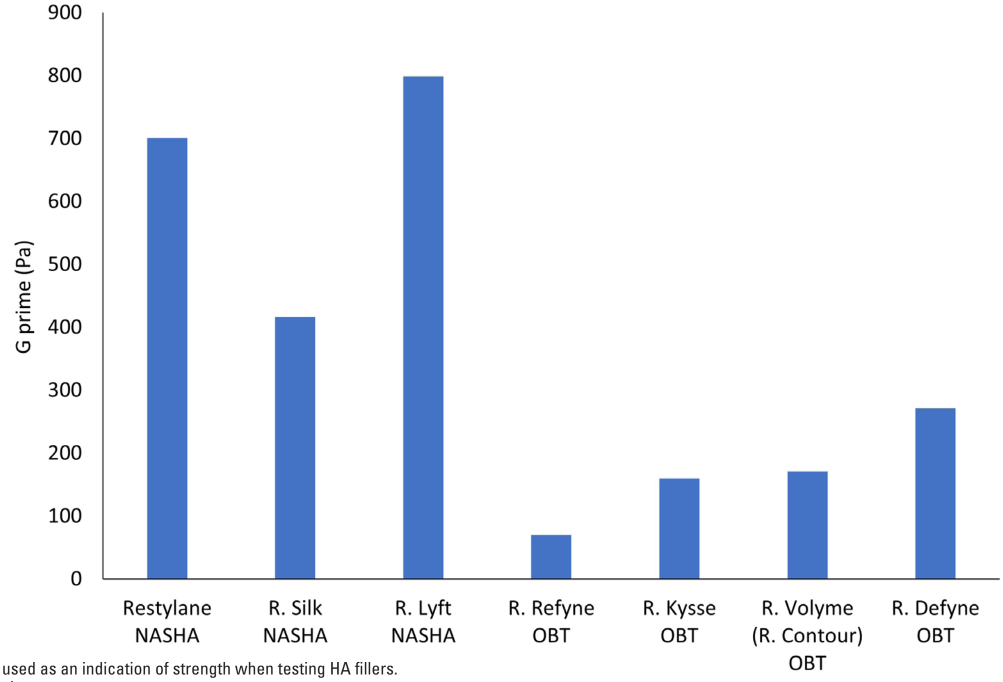
INTRODUCTION

The demand for minimally invasive aesthetic treatments, including hyaluronic acid (HA) fillers, has grown significantly in recent years, with the uptake of such procedures rising by more than 75% in the United States (US) over the past decade.[1,2] Clinician experience, expertise, and confidence in handling and administering these products have subsequently grown.[1,3] HA fillers provide a durable, yet non-permanent, non-surgical option to address facial volumetric changes associated with aging.[2,4-9] HA filler treatments in general aim to provide volume so that the face appears lifted while looking even and natural.[2,4-6]

HA gel strength/firmness is usually expressed as the elastic modulus, or G prime (G′), while flexibility can be defined by the xStrain (the strain value for the G prime/G double prime [G′′] crossover in the amplitude sweep).[2,10,11] The xStrain represents the furthest point at which the gel can recover following deformation.[2,11] Beyond this point, the gel begins to behave more like a liquid and will no longer be able to return to its original shape.[2,11] Because G prime and xStrain are two separate properties and not necessarily linked, products with similar G primes may exhibit different xStrains and vice versa.[12] Products with a higher G prime are stronger and more resistant to deformation than those with a lower G prime.[12] Products with higher xStrain are more flexible than those with lower xStrain values.[11,12]

The NASHA® technology, used for Restylane®, Restylane Silk (R. Silk), and Restylane Lyft (R. Lyft), allows for the preservation of the naturally long HA chains resulting in strong gels with high G primes. In addition, the NASHA technology uses minimal modification and controlled particle sizing.[11,13–17] HA fillers produced with NASHA exist both with and without lidocaine.[13,16,17] The OBT™ technology (referred to as XpresHAn in the US) produces flexible HA fillers where the strength/firmness (G prime) is varied by applying different degrees of crosslinking.[11,12,14,15,18–25] Fillers formulated using OBT include Restylane Refyne (R. Refyne), Restylane Kysse (R. Kysse), Restylane Defyne (R. Defyne), and Restylane Volyme (R. Volyme; Restylane Contour in the US).[19-22,25]

FIGURE 1. Elastic modulus (G prime) measurements for strength at 0.1 Hz for NASHA® and OBT™ formulations of Restylane hyaluronic acid fillers.



G prime measurements are used as an indication of strength when testing HA fillers.
HA, hyaluronic acid; R, Restylane.

Although measurement of flexibility is a well-established rheology method, xStrain as an indicator of flexibility for HA fillers was first applied to the OBT and NASHA gels.[11,26-28] Using the xStrain method, an amplitude sweep is conducted where the level of deformation (or % strain) is increased until the yield point at the end of the linear viscoelastic region (LVR) is reached, when the gel can no longer return to its original shape.[11] More flexible HA formulations can withstand high levels of strain before yielding.[11] The current study examined strength/firmness (G prime) and flexibility (xStrain) for the full range of NASHA and OBT HA fillers. In addition, this paper aimed to link these gel properties with clinical performance.

MATERIALS AND METHODS

G prime and xStrain

G prime (strength/firmness) and xStrain (flexibility) were measured for Restylane, R. Silk, and R. Lyft (NASHA gels) and R. Refyne, R. Kysse, R. Volyme, and R. Defyne (OBT gels) and performed in sequence, including a relaxation time of 30 minutes. A frequency sweep from 10 Hz to 0.1 Hz at 0.1% strain was followed by an amplitude sweep from 0.1% to 10,000% (0.001 to 100) strain at 1 Hz. The gap was 1 mm using a PP25 rheometric measuring system at 25°C. The frequency sweep was evaluated for G prime (G′), G double prime (G′′), G*, and tan delta (tan δ) at 0.1 Hz.

The amplitude sweep was first evaluated at 0.1% strain to verify that the applied frequency sweep strain was within the LVR. The strain was then evaluated at the crossover point of the amplitude sweep (where G prime and G double prime had the same value). This value denoted the xStrain.

RESULTS

HA fillers produced with NASHA technology demonstrated the highest G primes (strength/firmness). Restylane, R. Silk, and R. Lyft had G primes of 701, 416, and 799 Pa, respectively. Across the OBT formulations, G primes were 70 (R. Refyne),

TABLE 1.

Measures of Strength (G prime) and Flexibility (xStrain) for Restylane Hyaluronic Acid Fillers Formulated With Either NASHA or OBT

Product	G prime (Pa)	xStrain (%)
NASHA-based formulations		
Restylane	701	7
R. Silk	416	19
R. Lyft	799	17
OBT-based formulations		
R. Refyne	70	1442
R. Kysse	160	908
R. Volyme (R. Contour)	171	930
R. Defyne	271	761

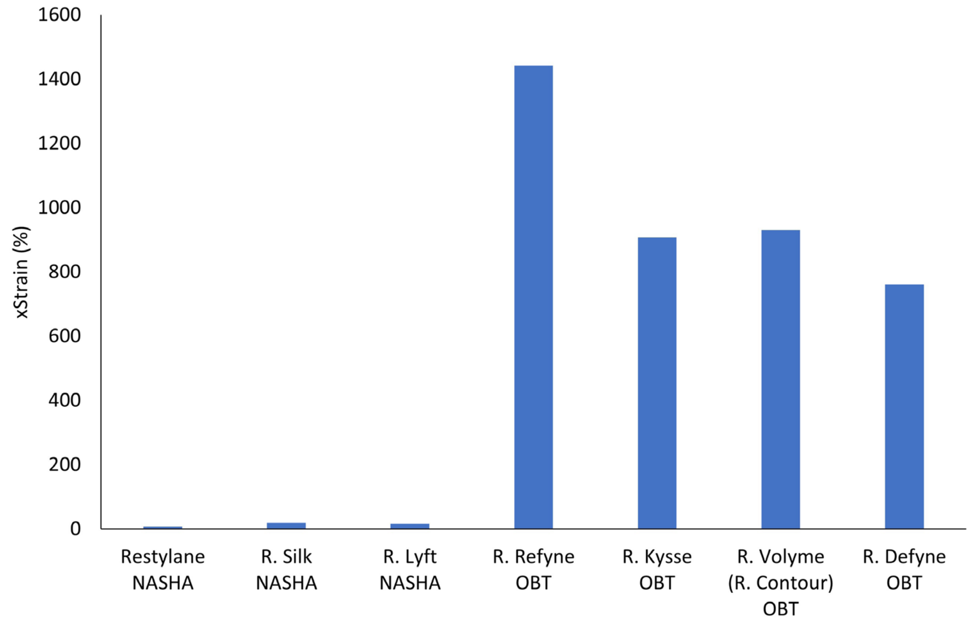
G prime measurements provide an indication of strength and xStrain measures flexibility when testing HA fillers. HA, hyaluronic acid; R, Restylane.

160 (R. Kysse), 171 (R. Volyme), and 271 (R. Defyne) Pa, respectively (Figure 1 and Table 1).

HA fillers produced with OBT technology demonstrated the highest xStrains (flexibility), comprising 1,442%, 908%, 930%, and 761% for R. Refyne, R. Kysse, R. Volyme, and R. Defyne, respectively. NASHA formulations showed xStrains of 7% (Restylane), 19% (R. Silk), and 17% (R. Lyft) (Figure 2 and Table 1).

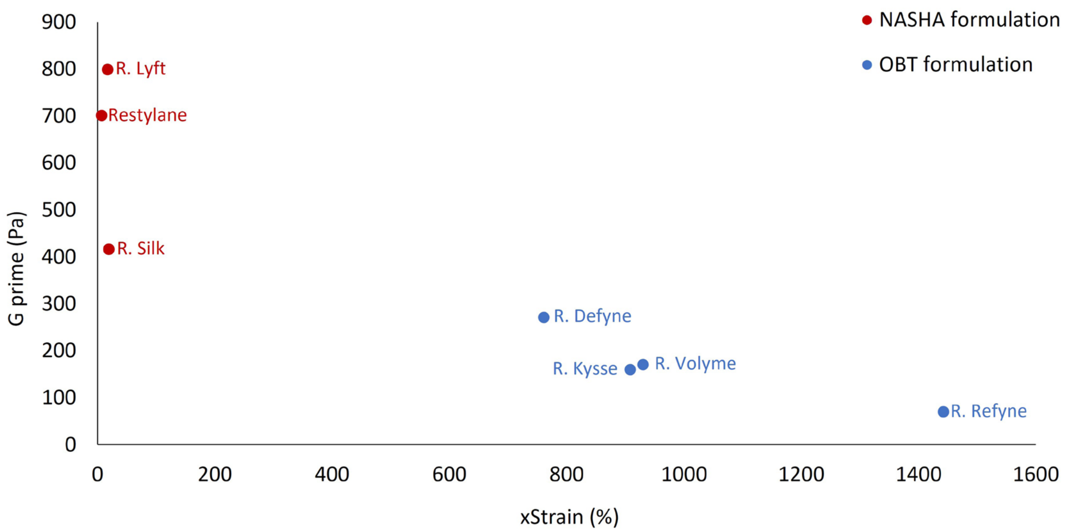
The combined characteristics of each HA filler in terms of strength/firmness (G′) and flexibility (xStrain) are plotted in Figure 3.

FIGURE 2. xStrain measurements for NASHA® and OBT™ formulations of Restylane hyaluronic acid fillers.



xStrain measurements are used as an indication of flexibility when testing HA fillers.
HA, hyaluronic acid; R, Restylane.

FIGURE 3. Strength (G prime) and flexibility (xStrain) balance for NASHA® and OBT™ formulations of Restylane hyaluronic acid fillers.



HA, hyaluronic acid; R, Restylane.

DISCUSSION

The data reported herein demonstrate a broad range in flexibility and strength/firmness for the HA fillers manufactured by the NASHA and OBT technologies. Among the variety of parameters used to differentiate HA fillers, both G prime and xStrain are based on accepted rheological measures, of which G prime may be the most widely used.[2,6,11] G primes for the Restylane fillers have previously been reported by, for example, Fagien et al (2019), Öhrlund et al (2018), and Lorenc et al (2017), and with similar results to what is reported herein.[6,11,29] However, G primes for two of the products produced by NASHA were slightly higher than previously reported.[6] In this study, respective G primes for Restylane and R. Lyft were 701 Pa and 799 Pa, compared with 544 Pa (Restylane) and 545 Pa (R. Lyft) reported by Fagien et al (2019).[6] A possible explanation may be slightly different instrumental settings as there is a lack of standard measurement guidance among different stakeholders.[29]

Access to a range of HA fillers with different physicochemical and rheological profiles provides the clinician with a toolbox of options that can be used to individualize and adapt aesthetic treatment according to personal requirements, facial structure, and desired outcome.[18,30,31] It is commonly suggested that clinicians must also have a good understanding of these properties to obtain optimum aesthetic results.[2,4,5,7–10,32,33] However, although there is a wide body of literature describing how physicochemical and rheological properties can be used to characterize different HA fillers, there are very few studies that correlate in vitro measurements with clinical performance.[6]

As reported in this study and previous studies, the NASHA technology typically produces strong/firm gels that are able to resist deformation.[6,12,33] Hence, these products are considered optimal for facial anatomical locations requiring precise projection, lift, or contouring. In a clinical setting, Di Gregorio et al (2022) demonstrated optimal aesthetic results with R. Lyft in the midface for subjects with thick tissue coverage and where the primary need for treatment was lifting or contouring.[18] Similarly, Jones et al (2020) showed improved aesthetic results for midface contouring with R. Lyft.[34] The high and precise projection capability of R. Lyft was demonstrated in a randomized and controlled clinical investigation showing R. Lyft to be effective in shaping the nasal dorsum and radix with aesthetic improvement maintained for up to 12 months.[35] Huang and Tsai (2020) also demonstrated long term aesthetic improvement and subject satisfaction (maintained over 24 months including one re-treatment) with both Restylane and R. Lyft used in multiple facial locations, including for example the midface, nose, and chin.[36]

As opposed to HA fillers based on the NASHA technology, HA fillers produced by the OBT technology are less strong/firm (softer, lower G prime) but highly flexible (high xStrain).[11] Softer gels may be less capable of resisting deformation compared with stronger/firmer gels, but greater flexibility allows them to tolerate deformation because they have the ability to return to their original shape once the strain is removed. Hence, a flexible gel is optimized for treating dynamic areas of the face (eg, nasolabial folds, marionette lines, and perioral regions including the lips) where an increased strain is applied during facial movements or expressions and removed when the face relaxes and returns to a static condition. Perceived naturalness of dynamic facial expression when the face was in motion was shown to be maintained or enhanced through 6 months following treatment of wrinkles and folds in the lower face, including nasolabial folds, marionette lines, and oral commissures, with R. Defyne or R. Refyne.[31,37] Percec et al (2020) used 3D digital imaging to show that R. Defyne and R. Refyne reduced the strain in most active facial expressions, and the changes in stretch and compression achieved resembled those of a more youthful face.[27] In addition, enhanced naturalness of the lower face when in motion was demonstrated after treatment with R. Defyne or R. Refyne in subjects with moderate to severe nasolabial folds and marionette lines.[26] Studies examining the use of R. Kysse in combination with R. Defyne and R. Refyne in the lips and perioral enhancement reported improved fulness, reduced wrinkle severity, and enhanced surface stretch, while natural movement and dynamic expression were maintained.[38-40]

CONCLUSION

Restylane HA fillers manufactured with NASHA and OBT Technologies displayed a wide range in both strength/firmness and flexibility. OBT products were highly flexible and lower in strength/firmness (with low to intermediate G prime), and have been shown to provide optimal clinical results in dynamic areas of the face such as nasolabial folds or lip region. By comparison, NASHA products were stronger (with higher G prime) but comparatively low in flexibility, conferring advantageous properties for targeted treatment to provide lift and projection in areas such as the nose and chin. These results provide a greater understanding of gel properties and how these properties translate to tissue performance to help guide clinicians in their selection of products for an optimal aesthetic outcome.

DISCLOSURES

Åke Öhrlund, Per Winlöf, Torun Bromée, and Inna Prygova are all employees at Galderma, Uppsala, Sweden.

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