

# Stabilized hyaluronic acid-based gel of non-animal origin, a promising new development for breast enhancement

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## Introduction

- The increased demand for minimally invasive procedures is driving the overall growth of the cosmetic industry. The search for improved volume-enhancing techniques has led to the use of a variety of solid implants and injectable materials for tissue augmentation procedures, including breast enhancement.
- Many investigated materials have significant associated drawbacks. Non-resorbable materials can accumulate permanently in the body and may cause granuloma formation or chronic foreign body reactions.<sup>1</sup> Complication and reoperation rates as high as 50% have been reported with silicone implants, during the first three years following surgery.<sup>2</sup> Fat transfer can provide substantial volume to deficient areas, but the costs are high and the surgery can be complex. A further criticism of fat transfer is its unpredictable efficacy.<sup>3</sup>
- A number of injectable, resorbable products based on hyaluronic acid are well established in facial esthetics.<sup>4,5</sup>
- To address the need for an injectable, biocompatible and resorbable product for body contouring and volume restoration, a new medical implant comprising hyaluronic acid-based gel of non-animal origin (NASHA™ gel) was developed by Q-Med AB, Uppsala, Sweden. Accordingly, two variations of Macrolane™ VRF received CE approval in 2007. Macrolane VRF30 is intended for use in areas where tissue cover is considered substantial (deep deposition), while VRF20 is intended for areas with thin tissue cover (more superficial deposition).
- In a pilot study of NASHA gel for breast enhancement (19 participants), mammograms and magnetic resonance imaging (MRI) were performed in 5 patients following treatment. Injected NASHA gel had increased radiolucency compared with silicone or saline implants, allowing visualization of tissue behind the gel. In addition, MRI results showed persistence of implanted NASHA gel up to 12 months post-injection, albeit with a degree of biodegradation.<sup>6</sup>

## Objective

- The objective of this study was to investigate the potential use of NASHA gel for female breast enhancement. Injection technique, efficacy and safety of the treatment were assessed.

## Materials & methods

- This study was approved by the ethical committee at the Karolinska Institute, Stockholm, Sweden.
- Study participants were non-pregnant, non-breast feeding women aged 25–50 years (n=20). They had to have small breasts (cup size A or B) and sufficient tissue cover, and be seeking enhancement of the shape and fullness of their breasts.
- The main exclusion criteria were: an unreasonable expectation regarding increase in breast volume, pathological findings on mammography/ultrasound, asymmetrical breasts, ptosis, hereditary risk of breast cancer, and previous breast augmentation or surgery.
- Participants were treated in groups of four to facilitate a step-wise approach for revision of the injection technique. In the first group of patients, NASHA gel was implanted under sterile conditions and following administration of general anesthesia. NASHA was administered at a single site via entry in the upper pole of the breast (anterior to the axillary line and adjacent to the pectoral muscle). In subsequent groups of patients the procedure was modified to optimize the technique.
- Each breast was lifted before introduction of the cannula to minimize injection into glandular tissue. A 12G (15 cm length) blunt cannula was then inserted. A small space was created centrally between the muscle and mammary gland prior to injection of the product. When in position, and whilst withdrawing the cannula, the NASHA gel was injected in the directions where volume was desired. If part of the implant did

not appear in the correct location, or in the case of unevenness, the breast could be massaged carefully to aid contouring of the gel with the surrounding tissues. A maximum of 100 ml of NASHA gel was injected per breast (Figure 1).

- MRI was used to determine the location and volume of injected NASHA, 1–5 days after treatment.
- In the case of unevenness or asymmetry, a touch-up procedure was performed 6–7 weeks after the initial treatment with an injection of up to 20 ml of NASHA gel per breast. A further MRI scan was carried out 0–10 days later.
- Patients, participating physicians and an independent evaluator rated breast improvement at 6 weeks, 3 months and 6 months by comparing pre- and post-procedure photographs and using the Global Esthetic Improvements Scale (GEIS).
- Safety was assessed by adverse event (AE) reporting and patient diaries.

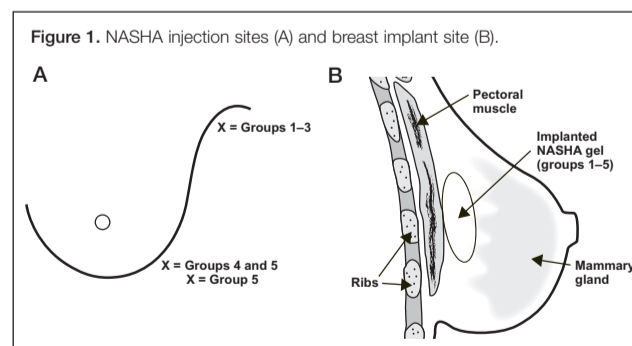
## Results

- Twenty women with a mean age of 37.2 years participated in the study. The average injection volume was 97.8 ml per breast.
- The first eight women were treated under general anesthesia, while application of a local anesthetic proved acceptable in the remaining twelve (Table 1).

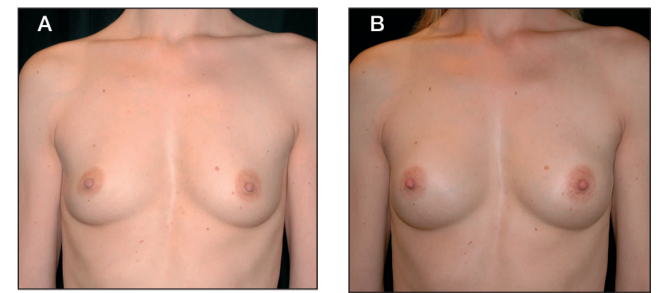
**Table 1.** Aspects of the injection procedure optimized during the study.

Group number	Anesthesia	Skin entry site (one per breast)	No. of sites of deposit
1	General	Upper pole, anterior to axillary line and adjacent to the pectoral muscle	One
2	General	Upper pole, anterior to axillary line and adjacent to the pectoral muscle	<b>A few deposits, placed through multiple passes</b>
3	<b>Local</b>	Upper pole, anterior to axillary line and adjacent to the pectoral muscle	A few deposits, placed through multiple passes
4	Local	<b>Lateral part of submammary fold</b>	A few deposits, placed through multiple passes
5	Local	Lateral part of submammary fold <b>or below</b>	A few deposits, placed through multiple passes

- Appropriate patient selection, accurate preoperative markings and thorough planning of the procedure were crucial for a good outcome.
- Important elements of the injection technique were found to be: lifting of the breast while inserting the cannula and while injecting the product; creating a space below the mammary gland before injecting; and injecting the product through multiple passes (to spread the product out in the space created), while still aiming for a single implant. The final eight subjects were injected from the lower lateral pole, by the breast inframammary fold (Table 1, Figure 1).

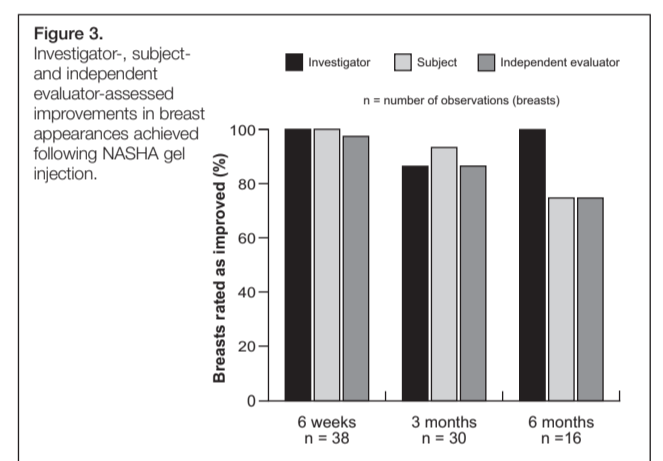


- The bevel of the cannula was held away from the pectoralis muscle, to avoid injection into tissue with low resistance. The previous pilot study had shown the potential for NASHA gel to migrate below the pectoralis muscle (5/19 cases); this was eradicated by holding the bevel away from the muscle.
- MRI scans 1–5 days after treatment demonstrated that, in 39 of the 40 breasts investigated, at least 80% of the implant was present in the correct location – between the pectoral muscle and the mammary gland (Figure 1).
- Touch-up was performed on one breast in a single patient (20 ml).



**Figure 2.** Study patient, before treatment (A) and 3 months after treatment (B).

- Mean implant volume at 1–5 days post-treatment and up to 14 days after touch-up was 102%, as determined by MRI scanning.
- Breast appearance was considered to be improved by 100% of patients at 6 weeks, 92% at 3 months and 75% at 6 months. Corresponding investigator-assessed GEIS improvement rates were 100%, 83% and 100%, respectively. Figure 2 indicates the typical visual improvement.
- Independent evaluators provided assessments of improvement that were similar to the patient assessments (Figure 3).



- Of the 20 subjects evaluated, 16 (80%) reported a total of 44 AEs. Twelve subjects reported 32 AEs that were related to either the study product or the injection procedure. The majority of these AEs (88%) were of mild to moderate intensity, with no cases of infection or inflammatory reaction.
- The most commonly reported AE, “injection site pain” (8 events), resolved within 8 days in all cases.
- The second most commonly reported AE was “implant site reaction” (6 events), referring to symptoms described as capsular contracture or capsular formation. Time to recovery was up to 133 days; with four of six encapsulations successfully treated with closed capsulotomy (none required surgical intervention).

## Conclusions

- A suitable injection technique for breast enhancement using NASHA gel, administered under local anesthesia, was developed in this study.
- NASHA gel injection was effective, with high breast improvement rates reported by participants and investigators at 6 weeks, 3 months and 6 months post-treatment. The treatment was also well tolerated, with no serious adverse events reported during the study.
- NASHA gel is a promising, biocompatible material for minimally invasive and well tolerated breast enhancement. Further studies are warranted to investigate the efficacy and safety of this material in larger patient groups.

## References

1. Lemperle G, Morhenn V, Charrier U. Human histology and persistence of various injectable filler substances for soft tissue augmentation. *Aesthetic Plast Surg* 2003; **27**: 354-66.
2. Cunningham B. The Mentor Core Study on Silicone MemoryGel Breast Implants. *Plast Reconstr Surg* 2007; **120**: 19S-29S.
3. Coleman SR. Structural fat grafting: more than a permanent filler. *Plast Reconstr Surg* 2006; **118**: 108S-120S.
4. Born T. Hyaluronic acids. *Clin Plast Surg* 2006; **33**: 525-38.
5. Gold MH. Use of hyaluronic acid fillers for the treatment of the aging face. *Clin Interv Aging* 2007; **2**: 369-76.
6. Tengvar M, Hedén P, Olenius M. Breast augmentation with stabilized hyaluronic acid-based gel of non-animal origin: visualization of tissue behind the implants. International Master Course on Aging Skin 2008, Paris.