The Canadian Experience with Fillers

Andrew E. Burchard, M.D.,[1] and David A.F. Ellis, M.D., F.R.C.S.C., F.A.C.S.[1]

ABSTRACT

The number of commercially available injectable soft tissue fillers has increased dramatically over the past decade. In the United States, a variety of temporary fillers have received Food and Drug Administration (FDA) approval. However, at the present time, there are no permanent soft tissue injectable fillers available. This article will discuss the authors' experience with some of the more popular soft tissue fillers on the market in Canada that are not currently available in the United States.

KEYWORDS: Injectable fillers, temporary, permanent

Soft tissue injectable fillers are becoming an integral part of a successful facial plastic surgery practice. The number of new products being released throughout the world each year is increasing at an exceptional rate, and physicians will often find themselves overwhelmed with information on which fillers are more effective than others. Surgeons must decide for themselves the products with which they are most comfortable and that ultimately give their patients the best cosmetic results. Certain regions of the world have far more products to choose from than do others. This article reviews several different fillers that are currently being used in Canada and are unavailable in American markets. The Health Protection Branch (HPB) in Canada approves fillers and is equivalent to the Food and Drug Administration (FDA) in the United States. We detail our experience with each of these materials to provide some insight on products that will likely be appearing in the United States over the next several years.

The authors have divided the products into three broad categories: *temporary*, lasting less than a year; *long term*, lasting more than a year, but not permanently; and *permanent*, lasting forever, but requiring occasional "touch-ups" as the aging process continues. It is also important to note that the longevity of the product is affected by the anatomic location in which it is placed. For example, material placed in the midcheek will last far longer than material placed in the lip-cheek groove due to the mechanical properties of each of these areas. In general, the more active and mobile an area is, the shorter the duration of effect by the product.

TEMPORARY SOFT TISSUE INJECTABLE FILLERS (LASTING LESS THAN 12 MONTHS)

Juvéderm Ultra with Lidocaine and Juvéderm Ultra Plus with Lidocaine

Juvéderm Ultra and Juvéderm Ultra Plus are both hyaluronic acid dermal fillers produced by Allergan, Inc. (Pringy, France) and have had FDA approval in the United States since 2006. Both products are composed of cross-linked hyaluronic acid, but the Ultra Plus formulation is more highly cross-linked than the Ultra formulation. Juvéderm Ultra with Lidocaine and Juvéderm Ultra Plus with Lidocaine were both released in Canada in October 2008 and are not currently available in the United States (Fig. 1). The physical properties of each are unchanged from their original formulations because the lidocaine hydrochloride is added as a salt and not as the local anesthetic fluid with which we are all

[1]Department of Otolaryngology–Head and Neck Surgery, University of Toronto, Toronto, Ontario, Canada.

Address for correspondence and reprint requests: David A.F. Ellis, M.D., F.R.C.S.C., F.A.C.S., Professor, Department of Otolaryngology–Head and Neck Surgery, University of Toronto, 167 Sheppard Avenue West, Toronto, Ontario, Canada M2N 1M9 (e-mail: drface @artoffacialsurgery.com).

Injectable Fillers; Guest Editor, Theda C. Kontis, M.D., F.A.C.S.

Facial Plast Surg 2009;25:129–134.

DOI 10.1055/s-0029-1220654. ISSN 0736-6825.

Figure 1 Juvéderm Ultra with Lidocaine and Juvéderm Ultra Plus with Lidocaine packaging.

familiar. Many physicians mix the product with their own local anesthetic in their offices, which is effective but ultimately changes the properties of the product. Allergan, Inc. estimates their products' longevity to be up to 12 months. As mentioned above, the longevity of the product is significantly affected by the anatomic location in which it is placed. Juvéderm placed in the cheeks can last 6 to 12 months, whereas Juvéderm placed in the lip-cheek groove may only last for 4 to 6 months.

Each 0.8-mL syringe is composed of 24 mg cross-linked hyaluronic acid, 3 mg lidocaine hydrochloride, and 1 g phosphate buffer. Juvéderm Ultra with Lidocaine is indicated for filling medium-sized depressions of the skin, contouring and volumizing facial wrinkles, and improving lip definition. Juvéderm Ultra Plus with Lidocaine is indicated for the correction of deeper skin folds and wrinkles. The product is easily injected with either a 27-gauge or 30-gauge needle for Juvéderm Ultra Plus and Juvéderm Ultra, respectively.[1]

In the author's experience, these products are extremely effective and easy to use. Injecting a small amount of the material at the injection site creates a tiny anesthetized area. The needle is then passed through this anesthetized area, and the stretching caused by the injection of subsequent product is virtually painless. Although this is beneficial in any area of the face that may be injected, it is truly revolutionary in the injection of lips. No additional local anesthetic is needed, allowing more accurate injections to be performed due to the lack of distorting effects caused by injecting the local anesthetic. Additionally, postinjection massage can be performed with minimal discomfort to the patient.

Teosyal

Teosyal represents a product line of seven different hyaluronic acid–based dermal fillers produced by Teoxane Laboratories (Geneva, Switzerland) that are currently unavailable in the United States. The concentrations of hyaluronic acid range from 15 to 25 mg/g and include both cross-linked and non–cross-linked formulations. This line of fillers is designed to be injected anywhere from the superficial to deep dermis, depending on the specific product used (Table 1). Teoxane Laboratories estimates the longevity of their products to range from 2 to 18 months.[2]

In the authors' experience, Teosyal Meso treatment for crepy skin had mixed results. Teosyal Meso is the hyaluronic acid formulation that has no cross-linking and is applied as multiple superficial intradermal injections into the skin. The neck area in a 69-year-old female patient was treated on a monthly basis for 4 months. There was an immediate effect of small nodules of the skin from the product itself that resolved within 24 hours. However, there was only minimal improvement of the crepy quality of the skin over the treatment period.

Airgent SMS

The Airgent SMS (Subdermal Minimal Surgery) system is a computer-controlled, pneumatically driven system used in the treatment of aging skin. The machine is composed of a console, handpiece, and disposable unit with specially formulated hyaluronic acid (Fig. 2). The console is very user friendly with adjustable settings for

Table 1 Teosyal Product Comparisons

	Teosyal 27G Deep Lines	Teosyal 30G Global Action	Teosyal 30G Touch-Up	Teosyal Meso
Presentation	Two 1-mL syringes	Two 1-mL syringes	Two 0.5-mL syringes	Two 1-mL syringes
Concentration	25 mg/g	25 mg/g	25 mg/g	15 mg/g
Type of needle	27 gauge	30 gauge	30 gauge	30 gauge
Injection site	Teosyal 27G is mainly recommended for filling deep facial wrinkles, increasing lip and cheek volume, and remodeling facial contours.	Teosyal 30G is mainly recommended to fill linear facial wrinkles, mild to moderate nasolabial folds, and to redefine lip contour.	0.5-mL syringes are particularly recommended for touch-up sessions when completing a treatment.	Teosyal Meso is a non–cross-linked hyaluronic acid. It is used to revitalize the skin on the face, neck, and neckline.
Injection level	Mid and deep dermis	Mid-dermis	Mid-dermis	Superficial dermis

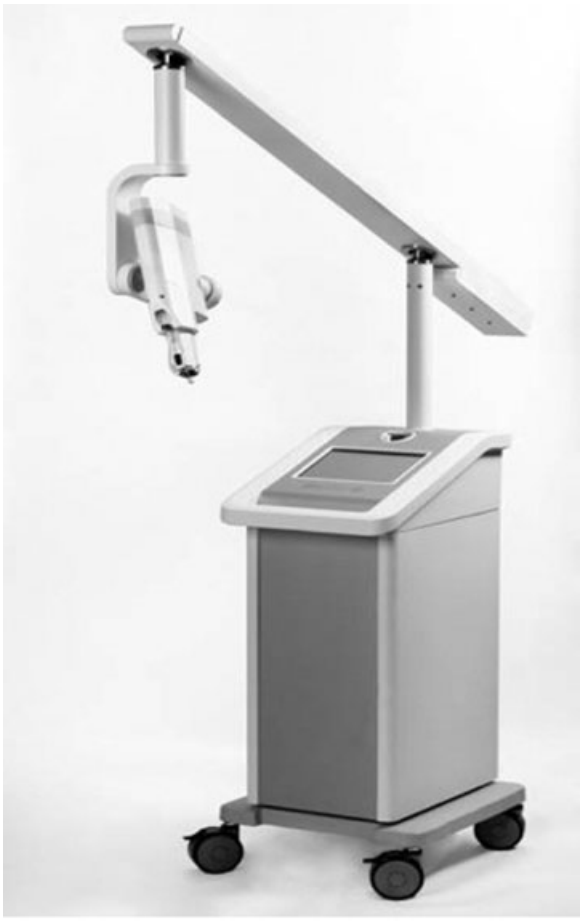

Figure 2 Airgent SMS console. (Reprinted with permission from PerfAction Ltd and Sigmacon Medical.)

treatment volume (100, 150, 200 mL of hyaluronic acid) and treatment pressure.

The machine functions by microscopically infusing a pneumatically accelerated jet of specific heavy hyaluronic acid molecules into the dermis. This jet of hyaluronic acid disperses laterally at high speed as "Nano Bullets" creating trauma and initiating the wound-healing process (Fig. 3). As the product disperses into the dermis, it attracts water molecules that thicken the dermis and reduce wrinkles as an immediate effect. The wound-healing process creates remodeling of collagen over several weeks and yields the machine's long-term effect. It is important to note that the filler in the Airgent is not intended to act in the same manner as conventional fillers. The hyaluronic acid is designed to create an immediate, temporary effect while the long-term mechanical result from dermal remodeling occurs.[3]

The skin appears nodular immediately after the treatment, but these usually resolve within 24 to 48 hours (Fig. 4). The Airgent system can be used to treat patients of all skin types and on most areas of the body, although it is specifically designed for treatment of the face, neck, and hands. Although most patients will see improvement after one treatment session, it is not uncommon for patients to require 3 or 4 treatments to obtain the best possible result.[3]

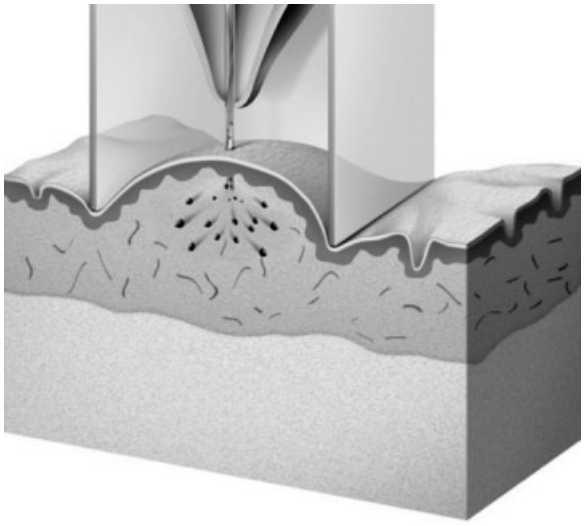

Figure 3 Airgent SMS system pneumatically injecting hyaluronic acid into the dermis inducing tissue injury. These ''Nano Bullets'' of hyaluronic acid disperse laterally and trigger the wound-healing process. (Reprinted with permission from PerfAction Ltd and Sigmacon Medical.)

LONG-TERM SOFT TISSUE INJECTABLE FILLERS (LASTING LONGER THAN 12 MONTHS)

Beautical-2 and Beautical-5

Beautical-2 and Beautical-5 are both manufactured by ProCytech (Martillac, France) and Rofil (Breda,

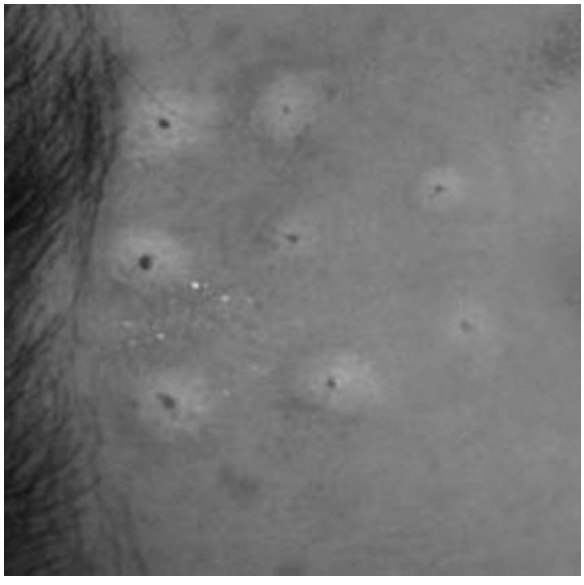

Figure 4 Nodular appearance of skin immediately after treatment with the Airgent SMS system. (Reprinted with permission from PerfAction Ltd and Sigmacon Medical.)

Figure 5 Beautical-2 and Beautical-5 packaging.

The Netherlands) and are composed of a cationic, hydrophilic copolymer of polyacrylamide gel particles creating a viscoelastic hydrogel (Fig. 5). The positively charged polymer particles attract negatively charged glucosaminoglycans, including hyaluronic acid, which causes the material to be held in the intended position. Unlike the permanent injectable fillers, Beautical induces minimal reaction from the surrounding tissue, and there is no fibrous capsule that forms around the product. Beautical-2 is designed to be injected into the mid and deep dermis with either a 27-gauge or 30-gauge needle, and it is estimated that 50% of the product remains at 2 years. Beuatical-5 is designed to be injected into or below the deep dermis into the subcutaneous plane with a 27-gauge needle, and it is estimated that 50% of the product remains at 5 years. Beautical-5 is manufactured at a higher temperature creating increased polymerization. As a result, Beautical-5 is broken down more slowly. It is preferable to undercorrect subdermal depressions and to perform any adjustment injections 4 to 6 weeks after the initial treatment.[4]

PERMANENT SOFT TISSUE INJECTABLE FILLERS

ArteSense

ArteSense, manufactured by European Medical Contract Manufacturing (Nijmegen, The Netherlands), is permanent filler composed of polymethylmethacrylate (PMMA) microspheres measuring 32 to 40 μm, blended with 3.5% collagen and 0.3% lidocaine (Fig. 6). After injection, the collagen suspension gets slowly reabsorbed over a 1- to 3-month period while the PMMA microspheres get encapsulated in fibrous tissue.[5] This process of encapsulation takes ~2 to 3 months to complete. Overcorrection of skin defects is not recommended. Successive treatments are usually performed every 2 to 3 months to optimize the cosmetic result, and up to 4 treatments may be required to fully correct a defect.

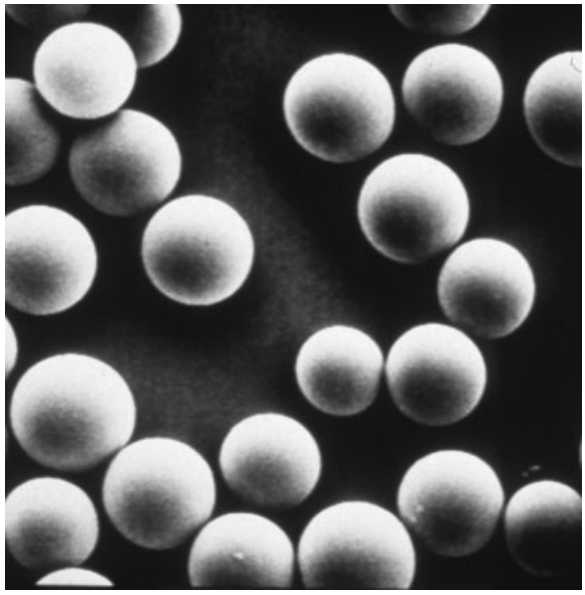

Figure 6 PMMA beads of ArteSense.

ArteSense is indicated for the long-lasting correction of deep wrinkles and other skin depressions. Injection in the lip for augmentation must be done carefully with proper control of product placement in the appropriate depth to avoid clumping and the formation of nodules.[6] Skin testing is recommended to elicit patients that are allergic to the collagen or lidocaine contained within the product. Contraindications to using ArteSense include sensitivity to collagen or bovine products, history of keloids, immune diseases, and atrophic skin. Caution should be exercised in patients with thin skin due to the risk of permanent surface irregularities. The lips are an area in which lumps can easily be seen. These irregular nodules can be treated with intralesional triamcinolone acetate injections to aid in their resolution. Most of these irregularities are related to injection technique and not to granuloma formation.[7]

Bio-Alcamid

Bio-Alcamid is manufactured by Polymekon (Brindisi, Italy) and distributed worldwide by Ascente Medical in Toronto (Fig. 7). It is a large-volume soft tissue filler composed of 96 to 97% hydrophilic polyalkylimide gel that is designed for facial contouring and the treatment of lipoatrophy and lipodystrophy.[8,9] Bio-Alcamid should be injected into the subcutaneous plane. A benign, low-grade inflammatory reaction occurs after the injection. The product can be molded and shaped into an ideal position over a 14-day period. During the next 45 days, an 0.2-mm thin fibrous capsule progressively develops around the injected material.[10] No significant giant cell reaction occurs.[11] Once the product is encapsulated, the implant remains soft to the touch. This product should not be confused with polyacrylamide gel that has a

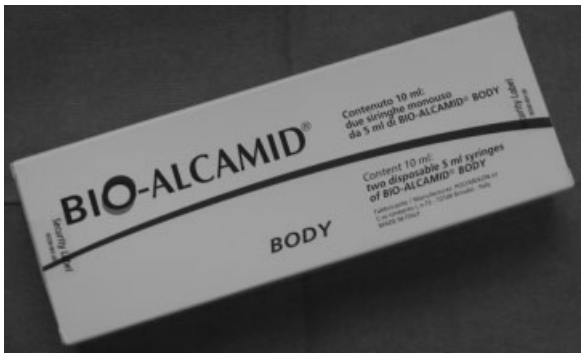

Figure 7 Bio-Alcamid packaging.

history of bad hypersensitivity reactions that are most difficult to treat. There are no reports of foreign-body granuloma formation with Bio-Alcamid.[12]

Although the product is permanent with respects to its biologic longevity, it is "reversible or adjustable" as the product can be removed via aspiration or puncture followed by drainage with manual pressure. This product is currently available in Canada and it may ultimately replace fat injections over time. In the senior author's experience of more than 70 patients, there has been a high rate of patient satisfaction. Regions treated include upper and lower midface lipodystrophy, the lip-cheek grooves, prejowl lipoatrophy, and drool grooves. It can also be used for malar and chin augmentation.

The injection is performed under local anesthetic at the injection site. Antibiotic coverage is initiated the day before treatment and is continued for a total of 5 days. The product is injected with a 14-gauge needle using a "quiet needle" technique to minimize bruising. Once injected, the product can be massaged to create uniformity to the desired effect filling in the gaps of the injection.

The patient returns 3 to 5 days later when the product can be further massaged to ensure an even and symmetrical distribution. Forty-five days later, when the capsule is fully formed, further adjustments can be made. Some patients may require further augmentation with the injection of more Bio-Alcamid. If further augmentation is required, the antibiotic must be re-prescribed. Other patients may require removal of product through a technique of needle puncture and massaging the product out through the needle tract.

Once the product has been placed, patients are advised to start prophylactic antibiotic coverage if a dentist is going to anesthetize the teeth and, in the process, pierce the capsule. The volumes of product used to augment areas of defect can range from 5 to 30 cm^3 per side depending on the subcutaneous fat depletion and the aesthetic goals of the procedure. Patient satisfaction is very high, and we have seen only one occurrence of infection. In a study of more than 2000 patient injections, 12 patients had infections (0.6% rate). All patients were successfully treated with anti-staphylococcal antibiotics and needle removal.[9]

In Canada, Bio-Alcamid is quickly becoming the subcutaneous replacement for fat transfer as it is performed under local anesthetic, with less postinjection bruising than is seen with fat transfer surgery.

CONCLUSION

New injectable fillers are being produced at an ever-increasing rate. Indeed, by the time this article is published, there will undoubtedly be new fillers attempting to break into North American markets. These products can be broadly categorized as temporary, long term, and permanent. Different patient populations prefer different longevities, and the plethora of product choices gives patients the opportunity to find the results they are seeking. However, it is becoming increasingly difficult for physicians to know the pro's and con's of the various products that are available. As new products are developed, it is incumbent on the provider to understand the differences between them and, ultimately, which choice will best suit the needs of his or her patient.

REFERENCES

1. Juvéderm Ultra with Lidocaine and Juvéderm Ultra Plus with Lidocaine [package inserts]. Pringy, France: Allergan Inc; 2008
2. Teoxane Laboratories. The best of hyaluronic acid: Teosyal. Available at: http://www.clarionmedical.com/uploaded/tiny_mce/File/Teosyal/Teosyal.pdf. Accessed December 19, 2008
3. Sigmacon Surgical Services. PerfAction Airgent SMS. Available at: http://www.sigmacon.co.uk/?product=59. Accessed December 19, 2008
4. Beautical-2 and Beautical-5 [package inserts]. Breda, The Netherlands: Rofil Inc; 2008
5. Cohen SR, Berner CF, Busso M, et al. Artefill: a long-lasting injectable wrinkle filler material—summary of the U.S. Food and Drug Administration trials and a progress report on the 4- to 5-year outcomes. Plast Reconstr Surg 2006;118(3 Suppl):64S–76S
6. Carruthers A, Carruthers JD. Polymethylmethacrylate microspheres/ collagen as a tissue augmenting agent: personal experience over 5 years. Dermatol Surg 2005;31(11 pt 2): 1561–1564
7. ArteSense [package insert]. Montreal, Canada: Canderm Pharma; 2008
8. Protopapa C, Sito G, Caporale D, Cammarota N. Bio-Alcamid in drug-induced lipodystrophy. J Cosmet Laser Ther 2003;5:226–230
9. Pacini S, Ruggiero M, Morucci G, Cammarota N, Protopapa C, Gulisano M. Bio-Alcamid: a novelty for reconstructive and cosmetic surgey. Ital J Anat Embryol 2002; 107:209–214
10. Ramires PA, Miccoli MA, Panzarini LD, Protopapa C. In vitro and in vivo biocompatibility of a polyalkylimide hydrogel for soft tissue augmentation. J Biomed Mater Res B Appl Biomater 2005;72:230–238

11. Formigli L, Zecchi S, Protopapa C, Caporale D, Cammarota N, Lotti TM. Bio-Alcamid: an electron microscopic study after skin implantation. Plast Reconstr Surg 2004;113:1104–1106

12. Claoue BL, Rabineau P. The polyalkylimide gel: experience with Bio-Alcamid. Semin Cutan Med Surg 2004;23:236–240