Fillers and Toxins
Updates and Practical Tips

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Mara Weinstein Velez, MD
S001 Finessing Surgical and Cosmetic Techniques

DISCLOSURES
I do not have any relevant relationships with industry
Overview

- Aging
- Toxins
  - Background
  - Updates
- HA Fillers
  - Background
  - Updates
Concepts in Facial Aging

- Not just gravity and sagging
- Atrophy and changes in bone, muscle, fat
- Complex ongoing alteration in proportion
- Not one large confluent layer of fat
- Multiple distinct compartments act independently
Beauty: Decline

- Patients looking to turn back clock
- More interested in addressing the new changes in their face than altering characteristics they have had since youth
- Want to look like themselves, just younger
- Help them become more self confident
- To feel beautiful is to be beautiful
The Magnificent 7: Defining facial Beauty

- Facial shape  ➔  Fillers, BTX-A
- Forehead height
- Eyebrow shape  ➔  Fillers, BTX-A
- Eye size and inter-eye distance
- Nasal shape  ➔  Fillers, BTX-A
- Lips  ➔  Fillers, BTX-A
- Skin clarity, texture & color  ➔  Lasers

Swift A, Remmington K BeautiPHIcation, Clin Plast Surg 2011
Trends

Injectables and noninvasive up 16%

Dermatologists do more than any other specialty.

- 1.7 million BTX-A
- 1.3 million fillers

ASDS Survey Data, 2015

TOXINS
Clostridium botulinum

- 1895 – Emille Pierre Van Ermengem
  - 34 Belgian citizens ill after salted ham
  - Causative organism in progressive paralysis known as botulism (Bacillus botulinus after sausage = botulus) “sausage poison”
  - Anaerobic, spore forming bacteria
Clostridium botulinum

- 1920 - Dr. Herman Sommer
  - Isolated toxins
  - Seven subtypes of exotoxin, A – G
    - All block neuromuscular signal
Overview of Botulinum Neurotoxins (BoNTs)

- **Potent** neurotoxins produced by *Clostridium botulinum*, gram-positive anaerobic bacteria\(^1\)
- 7 serotypes (A to G); each produces a distinct antigenic toxin (most commonly used aesthetic BoNTs are type A)\(^1\)

<table>
<thead>
<tr>
<th>US Trade Name</th>
<th>Generic Name</th>
<th>Serotype</th>
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<tbody>
<tr>
<td>BOTOX Cosmetic</td>
<td>OnabotulinumtoxinA</td>
<td>A</td>
</tr>
<tr>
<td>DYSPORT</td>
<td>AbobotulinumtoxinA</td>
<td>A</td>
</tr>
<tr>
<td>XEOMIN</td>
<td>IncobotulinumtoxinA</td>
<td>A</td>
</tr>
<tr>
<td>MYOBLOC</td>
<td>RimabotulinumtoxinB</td>
<td>B</td>
</tr>
</tbody>
</table>

**Similarities\(^2\):**
- Clostridial neurotoxin
- Di-chain structure
- Inhibition of acetylcholine release
- Produce temporary flaccid paralysis

**Differences:**
- Antigenically distinct
- Binding sites
- Enzymatic actions
- Pharmacology

Clostridium botulinum

- Botulinum toxin A (BTX-A)
  - most potent natural neurotoxin known
  - $10^{12}$ as potent as sodium cyanide
- FDA approval in 1979 for strabismus
  - 1980s Carruthers recognized reduced facial wrinkles in patients tx with blepharospasm
- FDA approval in 2002 for glabellar rhytides
  - Oculinum, Inc. acquired by Allergan 1989
  - Name changed to BOTOX
BoNT-A Molecular Structure

150-kDa polypeptides that consist of a 50 kDa light chain (red) and a 100 kDa heavy chain (blue) joined by a disulfide bridge (inset, yellow)

- Heavy chain docks on the presynaptic nerve terminal and also allows light-chain translocation across endosomal membrane
- Light chain cleaves SNAP-25 and prevents transmission of ACh across the neuromuscular junction localized paralysis of the muscle fiber

Botulinum Toxin Mechanism of Action

- Muscle weakness seen in 2 – 4 days after injection
- Full paralysis (complete weakness) at 7 – 10 days
- Lasts 3 – 4 months
BoNT-As: Pharmacologic Similarities & Differences: All same "active" **150 kD ingredient**

<table>
<thead>
<tr>
<th></th>
<th>BOTOX Cosmetic&lt;sup&gt;1&lt;/sup&gt;</th>
<th>DYSPORT&lt;sup&gt;2&lt;/sup&gt;</th>
<th>XEOMIN&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vial Size</strong></td>
<td>50 U, 100 U</td>
<td>300 U</td>
<td>50 U, 100 U</td>
</tr>
<tr>
<td><strong>Stabilization</strong></td>
<td>Vacuum-dried</td>
<td>Lyophilized</td>
<td>Lyophilized</td>
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<tr>
<td><strong>Composition</strong></td>
<td>C botulinum toxin type A</td>
<td>C botulinum toxin type A</td>
<td>C botulinum toxin type A</td>
</tr>
<tr>
<td></td>
<td>ATCC 3502 (Hall strain)</td>
<td>ATCC 3502 (Hall strain)</td>
<td>ATCC 3502 (Hall strain)</td>
</tr>
<tr>
<td></td>
<td>hemagglutinin complex</td>
<td>hemagglutinin complex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.25 mg HSA, 0.5 mg HSA</td>
<td>0.125 mg HSA</td>
<td>1.0 mg HSA (both vial sizes)</td>
</tr>
<tr>
<td></td>
<td>0.45 mg NaCl, 0.9 mg NaCl</td>
<td>2.5 mg lactose</td>
<td>4.7 mg sucrose (both vial sizes)</td>
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<tr>
<td><strong>Molecular weight</strong></td>
<td>900 kDa</td>
<td>500‒900 kDa</td>
<td>150 kDa</td>
</tr>
<tr>
<td><strong>Clostridial protein per 100 U</strong></td>
<td>0.73 ng⁴</td>
<td>0.65 ng⁴</td>
<td>0.44 ng⁴</td>
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<tr>
<td><strong>Specific biologic activity</strong></td>
<td>60 MU-E/ng⁵</td>
<td>100 MU-E/ng⁵</td>
<td>167 MU-E/ng⁵</td>
</tr>
<tr>
<td><strong>Storage (packaged product)</strong></td>
<td>36°F–46°F for 36 mo</td>
<td>36°F–46°F until vial expiration</td>
<td>68°F–77°F for 36 mo</td>
</tr>
<tr>
<td><strong>Storage (once reconstituted)</strong></td>
<td>36°F–46°F, use within 24 h</td>
<td>36°F–46°F, use within 4 h</td>
<td>36°F–46°F, use within 24 h</td>
</tr>
<tr>
<td><strong>On-label aesthetic indications</strong></td>
<td>Glabellar lines associated with corrugator and/or procerus muscle activity in adult patients; lateral canthal lines associated with orbicularis oculi activity in adult patients</td>
<td>Glabellar lines associated with procerus and corrugator muscle activity in adult patients &lt;65 years of age</td>
<td>Glabellar lines associated with corrugator and/or procerus muscle activity in adult patients</td>
</tr>
</tbody>
</table>

HSA, human serum albumin, MU-E, MU-E: equivalence mouse units

How are they Different?

- Complexing proteins around 150 BTX-A
- Xeomin has none
- Botox has 900 kDa complex
- Dysport has a 500 – 900 kDa complex
Complexing proteins

Multi-protein complex protects the polypeptide

- Do not affect diffusion of active neurotoxin compared with free form\(^1,2\)
- Do not contribute to stability in aesthetic use\(^1,2\)
- May be associated with secondary nonresponse caused by development of neutralizing antibodies\(^3\)

- NaCl disrupts and frees 150 kD
- 85% of neurotoxin in free form in less than 1 minute
- **We are likely injecting free form**

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## BoNT-A Preparation & Use

<table>
<thead>
<tr>
<th>On-label</th>
<th>Off-label*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BOTOX Cosmetic</strong>&lt;sup&gt;1&lt;/sup&gt; (100 U vial)</td>
<td><strong>BOTOX Cosmetic</strong>&lt;sup&gt;1&lt;/sup&gt; (100 U vial)</td>
</tr>
<tr>
<td><strong>DYSPORT</strong>&lt;sup&gt;2&lt;/sup&gt; (300 U vial)</td>
<td><strong>DYSPORT</strong>&lt;sup&gt;2&lt;/sup&gt; (300 U vial)</td>
</tr>
<tr>
<td><strong>XEOMIN</strong>&lt;sup&gt;3&lt;/sup&gt; (100 U vial)</td>
<td><strong>XEOMIN</strong>&lt;sup&gt;3&lt;/sup&gt; (100 U vial)</td>
</tr>
<tr>
<td>Preservative-free saline</td>
<td>Preserved saline</td>
</tr>
<tr>
<td>2.5 mL diluent volume</td>
<td>1.0 mL – 5.0 mL diluent volume</td>
</tr>
<tr>
<td>Use within 24 h</td>
<td>Use within 7–10 d</td>
</tr>
<tr>
<td>Single patient use vial</td>
<td>More than 1 patient per vial</td>
</tr>
<tr>
<td>Preservative-free saline</td>
<td>Preserved saline</td>
</tr>
<tr>
<td>2.5 mL or 1.5 mL diluent volume</td>
<td>1.0 mL – 6.0 mL diluent volume</td>
</tr>
<tr>
<td>Use within 4 h</td>
<td>Use within 7–10 d</td>
</tr>
<tr>
<td>Single patient use vial</td>
<td>More than 1 patient per vial</td>
</tr>
<tr>
<td>Preservative-free saline</td>
<td>Preserved saline</td>
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<tr>
<td>0.5 mL – 8.0 mL diluent volume</td>
<td>1.0 mL – 6.0 mL diluent volume</td>
</tr>
<tr>
<td>Use within 24 h</td>
<td>Use within 7–10 d</td>
</tr>
<tr>
<td>Single patient use vial</td>
<td>More than 1 patient per vial</td>
</tr>
</tbody>
</table>

*With appropriate storage and safety measures

Units of Measurement

- No dose standardization (potency units not interchangeable)
  - Each BoNT’s potency measured with proprietary mouse LD_{50} assay protocol\(^1\-\!^4\)
  - Different dosing, injection patterns, and injection techniques may be needed to ensure natural results with all products\(^5\)
- **Approximate** conversion factor for DYSPORT* and BOTOX from published studies:
  2.5 – 3 DYSPORT U ≈ 1 BOTOX U\(^6\-\!^8\)
- BOTOX and XEOMIN generally considered equivalent\(^9\)
  - 1 BOTOX U ≈ 1 XEOMIN U
- For best outcomes for any product, use clinical trial data, consensus guidelines, and personal experience as a guide

BTX-A Cosmetic Sites of Injection

- Upper face
  - Glabella
  - Forehead
  - Periorbital
  - Bunny lines
- Lower face
  - Perioral
  - Chin
  - Jawline
  - Neck
BTX-A: Most common sites of injection

- Glabella
- Forehead
- Crows Feet

Before

After

Before Botox

After Botox

PereaMD

BOTOX Before (Above), After (Below)
Don’t forget the lower face...

**Gummy Smile:**
- ≥2 mm of gingival exposure with smiling
- Hyperactivity of the lip elevators (levator labii superioris alaque nasi, levator labii superioris & zygomaticus minor)
- Inject 3-5mm lateral to each nostril

**Masseter muscle:**
- Hypertrophy can contribute to a heavy appearance of the lower face
- 1st reported in the Korean literature
- Few treatments spaced a few month apart
- Palpate with the patient actively clenching to delineate anterior and posterior borders
- 3-6 injections into the belly

Giordano, Matarasso, Ozog. Injectable and topical neurotoxins in dermatology: Indications, adverse events and controversies. JAAD. 2017
Nefertiti lift

• Injections of BTX-A along the inferior border of the mandible and the platysmal bands

• Most helpful in younger patients with platysma muscle hyperactivity and retained skin elasticity

1. 4 injections 1-2cm apart under the mandibular border

2. Platysmal bands injected in a vertical series 2-4cm apart

3. Hold band between thumb and index finger, 5U, 125U max

4. 15 day FU for retouching

Nefertiti Lift Video

http://links.lww.com/PRS/C193
Current Issues
More vs. less injection points

- Needle issues with patients
- Less pain?
- Less side effects?
- Faster treatment times?
More vs. less injection points

- 1 vs. 3 injection points along lateral canthal area
- 36 U ABO to each side
- Primary endpoint: difference of efficacy at maximal contraction; Secondary endpoint: difference in side effect profile

More vs. less injection points

- 35 women, 5 men – 0, 7 \( \rightarrow \) 120 days post treatment
- No significant difference among treated sides, side effects
- Trend (not statistically significant) toward prolonged efficacy of the 1 injection site
- No mention of any asymmetry or brow positioning

Does placement Matter
Subcutaneous vs. Intramuscular

Accuguide injection electromyographic (EMG) device attached to needle

Subcutaneous vs. Intramuscular

- **Study:** Gordin et al.
  - **Split Face - subcutaneous vs intradermal**
  - **Frontalis 12 U ONA, 4 injection points**
  - **No difference in eyebrow height 2 weeks, 4 weeks, 4 months**
  - **No difference in side effects except pain during injection less with subcutaneous**

Treating Millennials
“Is it too early?”

• Prejuvenation
• Common question in practice
• Etched lines from repeated muscular use
• Don’t use, Don’t form lines
• Low dose to soften and prevent, not ‘freeze’
• Other early intervention that we already encourage- sunscreen, retinoids.

Case Report: Binder

- 38 year old, Identical Twins
  - one with repeated neuromodulator (3-4 x per year to forehead/glabella over 13 years, and 2x to crows feet in last 2 years)
  - Other twin only twice over 13 years to forehead/glabella
  - Greatly diminished dynamic and etched rhytides

Other studies:
- HA filler shown to stimulate collagen production
- Increased collagen production after IPL, fractional nonablative, etc.

The minimally treated twin (A, B, and C) and the regularly treated twin (D, E, and F). Hyperfunctional lines in the forehead (B and E) and glabellar regions (C and F) are visible in the minimally treated twin but not in the regularly treated twin.
Mantox, BroTox, XeoMen

- Men undergoing cosmetic procedures continue to rise
  - Between 1997-2014, increased 273%
- Larger facial muscles, requires higher doses of BoNT-A to achieve same cosmetic result as females
- Avoid arching brow when treating frontalis
  - Equal medial and lateral injections
- Inferior fanning pattern of crow’s feet
  - Superficial Microdroplet technique to avoid zygomaticus major
Future Toxins
Topical BTX-A

  - 36 pts, double blinded, randomized
  - crow’s feet, RT001 30 min, again wk 4
  - wk 8: 50% showed at least 2 pt improv.
  - wk 8: 95% showed at least 1 pt improv.
  - pt assessment: 84% vs 41% placebo

  - 90 pts, double blinded, randomized
  - crow’s feet, RT001 30 min
  - wk 4: 44% showed at least 2 pt improv.
  - Wk 4: placebo = 2.3% with 2 pt improv.
  - wk 4: 89% showed at least 1 pt improv.
  - marked clinical: 58% vs 4.7% placebo
RT001 (daxibotulinumtoxin A) topical gel

- Phase III clinical trial
  - 450 pts, Randomized, double-blind
  - Crows feet, RT001 30min vs. Placebo
  - Weeks 0, 4
  - Did not achieve endpoint of 2pts or greater improvement between baseline and 28 days after treatment
RT002 (daxibotulinumtoxin A)-Injectable, Presented at AAD 2016

- Phase 2 Study to determine the safety and efficacy of daxibotulinum toxin A at three doses for glabellar lines vs OnaBoNTA vs placebo
- Placebo controlled, randomized, double-blinded multicenter (9) sites
- To assess duration of single treatment vs OnaBoNTA vs placebo
- N= 268, 1:1:1:1:1 randomization
  - 20 u OnaBoNTA, 20 u RT002, 40 u RT002, 60 u RT002, placebo
- Followed for 24-26 wks or until return to baseline score
RT002 (daxibotulinum toxin A)

- RT002 had higher response rate vs OnaBoNTA of > 1 pt improvement on severity score beginning at week 2 thru week 24

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Week 16</th>
<th>Week 20</th>
<th>Week 24</th>
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<tbody>
<tr>
<td>RT002 40U</td>
<td>100%</td>
<td>100%</td>
<td>100%*</td>
<td>95%</td>
<td>79%*</td>
<td>59%*</td>
<td>36%</td>
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<tr>
<td>Onabot 20U</td>
<td>98%</td>
<td>95%</td>
<td>90%</td>
<td>86%</td>
<td>54%</td>
<td>32%</td>
<td>19%</td>
</tr>
</tbody>
</table>

- 6 mo duration of > 1 pt improvement on IGA-FWS w 40 u RT002
  - 23.6 wks vs 18.8 wks (OnaBoNTA O)
  - 40 u RT002, no ptosis, most favorable profile

RT002 (daxibotulinum toxin A)

- Phase 3 development
- DaxibotulinumtoxinA (40U) compared to onabotulinumtoxinA (20U)
  - Moderate to severe glabellar lines at maximum frown

- Longer median duration of response, \( p = 0.030 \)
  - DaxibotulinumtoxinA (40U): 24 weeks
  - OnabotulinumtoxinA (20U): 19 weeks
FILLERS
Hyaluronic Acid (HA) Fillers

- Naturally occurring polysaccharide polymer that retains water
  - 1g HA can bind up to 6 L H$_2$O$^1$
- Natural component of the skin – hydrates, lubricates, stabilizes connective tissue$^{2,3}$
- Nonallergenic – same molecule across all mammalian species
- Natural look and feel
- Revisable
  - Dissolves over 6–24 mos depending on filler
  - Can be dissolved with hyaluronidase
- Safe for use in Fitzpatrick skin types IV, V, and VI$^{5-7}$
  - No significant risk for hypopigmentation, hyperpigmentation, scarring, keloid formation

HA Stabilization, Cross-linking, Gel Hardness ($G'$)$^{1-4}$

- Naturally-occurring HA has short half-life and must be cross-linked before use as soft tissue filler
- Degree of cross-linking and HA concentration effect elastic modulus ($G'$) ability to resist deformation
  - Higher $G'$ = firmer, harder, more elastic than gel with lower $G'$ generally

After Crosslinking, gels must be broken down in order to be injected

- **Homogenization vs. Sieving**
- Homogenization produces *monophasic* particles of same size, and smooth consistency, and softer gels with lower $G'$
- Sieving produces *biphasic* gels of differing sizes, granular consistency, and harder gels with higher $G'$
<table>
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<tr>
<th>Trade Name</th>
<th>HA Conc., mg/mL</th>
<th>Type</th>
<th>Lidocaine</th>
<th>Needle Size, G</th>
<th>US FDA Approval</th>
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<tr>
<td>Belotero Balance</td>
<td>22.5</td>
<td>Cohesive Polydensified Matrix HA</td>
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<td>27 or 30</td>
<td>2011</td>
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<td>Juvéderm Ultra</td>
<td>24</td>
<td>Hylacross HA</td>
<td>No</td>
<td>30</td>
<td>2006</td>
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<tr>
<td>Juvéderm Ultra Plus</td>
<td>24</td>
<td>Hylacross HA</td>
<td>No</td>
<td>27</td>
<td>2006</td>
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<td>Juvéderm Ultra Plus XC</td>
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<td>Juvéderm Voluma</td>
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<td>Vycross HA</td>
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<td>Juvederm Volbella</td>
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<td>Vycross HA</td>
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<td>Restylane</td>
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<td>NASHA</td>
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<td>2014 (lips, perioral rhytids)</td>
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<td>Restylane Defyne</td>
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<td>XpresHAn</td>
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<td>27</td>
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<tr>
<td>Restylane Refyne</td>
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<table>
<thead>
<tr>
<th>Product</th>
<th>Elasticity* G’</th>
<th>Viscosity* G”</th>
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<tbody>
<tr>
<td>Radiesse</td>
<td>1,407</td>
<td>349,830</td>
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<tr>
<td>Radiesse (+) integral lidocaine</td>
<td>1,165</td>
<td>310,305</td>
</tr>
<tr>
<td>Restylane-L</td>
<td>565</td>
<td>131,310</td>
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<tr>
<td>Restylane-Lyft</td>
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<td>127,090</td>
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<tr>
<td>Restylane</td>
<td>513</td>
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<td>Juvéderm Voluma</td>
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<td>BELOTERO BALANCE</td>
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<td>9,217</td>
</tr>
<tr>
<td>Juvéderm Ultra</td>
<td>28</td>
<td>7,307</td>
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</tbody>
</table>

*All measured at 0.7 Hz (physiologically relevant for stresses common to skin) NA, not available

NKOTB

- Refyne, Defyne
- (Voluma), Vollure, Volbella
Refyne, Defyne

- FDA indication:
  - Restylane® Refyne is indicated for injection into the mid-to-deep dermis for correction of moderate to severe facial wrinkles and folds (such as nasolabial folds) in patients over the age of 21
  - Restylane® Defyne is indicated for injection into the mid-to-deep dermis for correction of moderate to severe deep facial wrinkles and folds (such as nasolabial folds) in patients over the age of 21
- Same as other Restylane products
  - Difference is in degree of crosslinking

Refyne/Defyne

Starts with 20 mg/mL HA gel

Variable amounts of cross linking

- **Refyne**, less cross linking, smaller particle size, lower lifting capacity, more flexible
- **Defyne**, more cross linking, larger particle size, more volume and definition, less flexible

Sizing: Gels pressed through screens for consistent texture

Data on File. Galderma Laboratories, L.P.
XpresHAn™ TECHNOLOGY ALLOWS NATURAL EXPRESSION IN MOTION

1.5 mL of Restylane Refyne in nasolabial folds, and 1.0 mL Restylane Refyne in marionette lines.

2.5 mL of Restylane Lyft in cheeks, 1.0 mL of Restylane Defyne in nasolabial folds, and 1.0 mL Restylane Refyne in marionette lines (touch-up).

1.0 mL of Restylane Defyne in nasolabial folds, and 1.0 mL Restylane Defyne in marionette lines.

Actual patients. Results unretouched. Individual results may vary.
Voluma, Volbella, Vollure

- **FDA Indication:**
  - JUVÉDERM VOLUMA® XC injectable gel is for deep injection in the cheek area to correct age-related volume loss
    - In practice – used to add volume to the chin, cheeks, and jawline. This is the most robust out of the 3. (Lasts up to 18-months.)
  - JUVÉDERM VOLLURE™ XC injectable gel is for injection into the facial tissue for the correction of moderate to severe facial folds (such as nasolabial folds)
    - The most versatile (Lasts up to 15-months.)
  - JUVÉDERM VOLBELLA® XC injectable gel is for injection into the lips for lip augmentation and for correction of perioral lines
    - In practice – used for delicate textural enhancements. Works beautifully for the lips, lip-lines, etc. (Lasts up to 12-months.)

- **Vycross vs. Hylacross Technology**
Voluma, Vollure, Volbella

- Lower concentrations of HA (vs. 24mg/ml)
  - 20 mg/mL HA Voluma
  - 17.5 mg/mL HA Vollure
  - 15 mg/mL Volbella

- Vycross – crosslinking technology with mixture of high and low MW HAs and BDDE (cross linking agent)
  - Tightly crosslinked

- Less hydroscopic given lower [HA] and tighter cross link than predecessor products

- Cohesivity increases with increasing [HA]
  - volbella < vollure < voluma

- Tissue integration
- Monophasic, homogenized
Current Concepts in the Use of Voluma, Volift, and Volbella

Gregory J. Goodman, FACD, MD
Arthur Swift, MD, CM, FRCS(C)
B. Kent Remington, MD, FRCP

Table 1. Vycross and Hylacross Comparative Rheological Parameters

<table>
<thead>
<tr>
<th>Agent</th>
<th>Concentration (mg/mL)</th>
<th>G Prime (Hardness)</th>
<th>Cohesivity (gm Force)</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voluma</td>
<td>20</td>
<td>398 Pa</td>
<td>40 gmf</td>
<td>Structure, volume, lift</td>
</tr>
<tr>
<td>Volift</td>
<td>17.5</td>
<td>340 Pa</td>
<td>30 gmf</td>
<td>Volume, contouring, lines</td>
</tr>
<tr>
<td>Volbella</td>
<td>15</td>
<td>271 Pa</td>
<td>19 gmf</td>
<td>Superficial spread</td>
</tr>
<tr>
<td>Juvederm Ultra</td>
<td>24</td>
<td>207</td>
<td>96 gmf</td>
<td>Definition</td>
</tr>
<tr>
<td>Juvederm Ultraplus</td>
<td>24</td>
<td>263</td>
<td>112 gmf</td>
<td>Form, volume</td>
</tr>
</tbody>
</table>

gmf, gram force.

Table 2. Indications for Vycross Products*

<table>
<thead>
<tr>
<th>Product</th>
<th>Indications Upper Face</th>
<th>Indications Midface</th>
<th>Indications Lower Face</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voluma</td>
<td>Temples, forehead, and acne scars (superficial injections) Eyebrow shaping</td>
<td>All areas of cheek including medial, lateral malar, submalar, cheek apex and preauricular areas, nasolabial folds (deep pyriform fossa injection), acne scars, nose dorsum, and nasal projection Radix and nasal bridge-lift nasal tip</td>
<td>Jaw angle, jawline, prejowl sulcus, chin reflation, and acne scars Lateral oral commissures, reflating marionette zone</td>
</tr>
<tr>
<td>Volift</td>
<td>Forehead volume and lines, eyebrow projection, A Frame of upper lid, and temples</td>
<td>Mid cheek accordion lines, layering for cheek volume with Voluma, nasolabial folds mid nose contouring (dorsum nasal tip, alar rim contouring)</td>
<td>Marionettes, perioral cutaneous, and vermilion Philtral columns</td>
</tr>
<tr>
<td>Volbella</td>
<td>Periorbital, tear trough, glabella, and forehead lines (intradermal injection)</td>
<td>Fine lines cheeks and maybe deeper periorbital lines</td>
<td>Vermilion and perioral areas, fine upper lid lines, and ear lobes</td>
</tr>
</tbody>
</table>

*GMF is the treatment of choice for an area, entries are bolded.
What to Use? - Not one universal
What to Use?

- Location on face?
  - Static or dynamic area?
- Volume deficiency or wrinkle/line fill?
- Thickness of skin in area to be injected?
- Do you want smooth tissue integration or a cohesive product that stays where you put it?
- Duration of HA?
  - Any co-morbid conditions in patient
  - Poor dentition, autoimmune conditions
  - Tighter/higher crosslinked- more difficult to dissolve?
0.5cc’s Juvederm Ultra, 0.5cc’s Volbella spaced 2 weeks apart
Practical Tips to avoid Adverse Events

- Inject slowly
- Inject perpendicular to vessels
- Stop immediately if any blanching is noted
- Keep the needle moving while injecting
- Deposit small aliquots

Know your anatomy!
**FIGURE 2.** Injection techniques: linear threading, serial puncture, and fanning.

2a) **Retrograde Threading**
Once the needle or microcannula is inserted, it is withdrawn while filler is injected like a thread in its track.

2b) **Anterograde Threading**
The filler is injected like a thread ahead of the needle while it is advanced forward during the injection.

2c) **Serial Puncture**
Once the needle is inserted, it remains static during the injection. Multiple closely placed beads of filler are then massaged gently into a continuous line.

2d) **Fanning**
Like retrograde threading, filler is injected while the needle or microcannula is withdrawn. Without being removed, its direction is changed and filler is injected as multiple threads in a wheel spoke pattern.
The storage debate

The Sterility of Partially Used Hyaluronic Acid Fillers after Long Storage.
The Sterility of Partially Used Hyaluronic Acid Fillers after Long Storage

- 36 used syringes, recapped, stored at room temp. mean duration 57.8 months (32.87-71.57)
- Prep: povidone iodine + 7-% isopropyl alcohol
- Invitro testing for microbes (anaerobic/aerobic), mycobacteria, fungi
- 5+ bacterial cultures (Staph. Epidermidis (3), Corynebacterium, Bacillus) – after 46.9 months

The Sterility of Partially Used Hyaluronic Acid Fillers after Long Storage.
Conclusions – Sterility of Partially used HA fillers

- Gram positive bacteria
  - Contamination from normal skin flora

**Recommendations:**

- Strict cleansing practices
- Keep rubber cap sterile and re-cap
- Deeper injections first to reduce risk of biofilms with reuse
- Discard <0.05ml of HA prior to injecting at touch up visit
Thank you for your attention!