Soft Tissue Fillers: Clinical Applications

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UNIVERSITY OF ILLINOIS
Hospital & Health Sciences System
Changing medicine. For good.

Disclosures

Merz Aesthetics- Advisory Board

AxcelRx Pharmacuticals - Advisory Board

Suneva Medical - Instructor

Will discuss off-label uses

Will use brand names for ease of understanding

Objectives

- Understand basic facial aging assessment
- Compare differences between fillers
- Identify anatomic sites for injection
- Learn to avoid & manage complications
- Review regulatory issues

Fillers Used & Locations

Most Common Sites

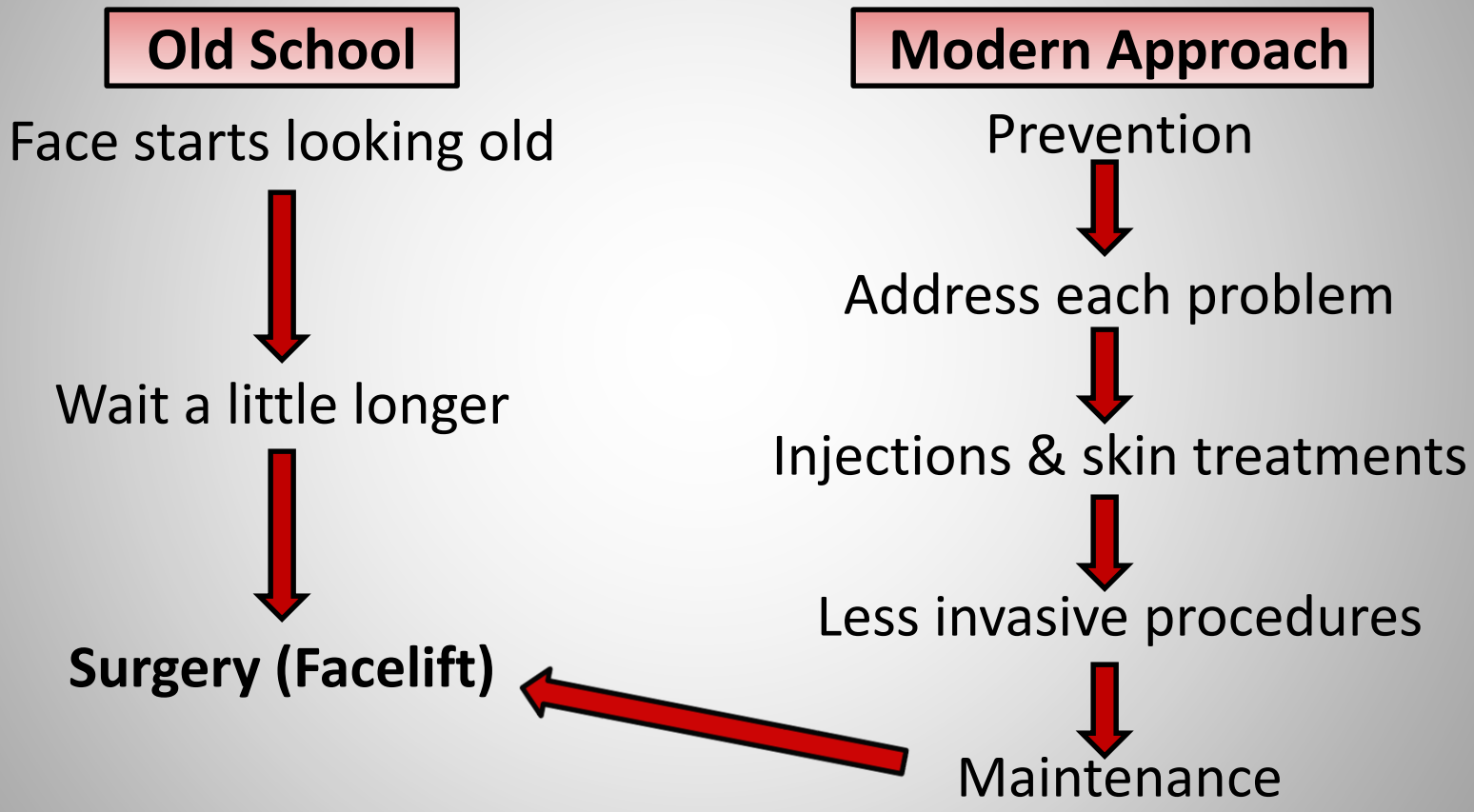
- Malar & cheeks
- Lips & perioral
- Tear troughs & periorbital
- Nasolabial folds
- Temples, hands, nose

Most Common Filler

- Radiesse
- Restylane products
- Bellafill
- Juvederm products
- Belotero
- Sculptra

Understanding Facial Aging

New Concepts



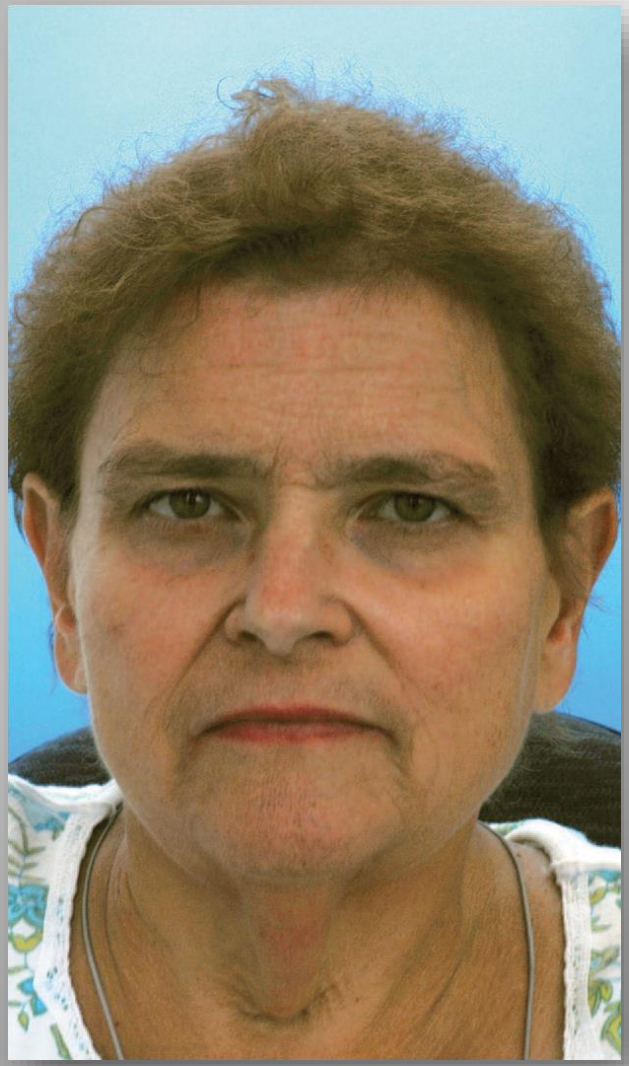
What Happens with Aging?

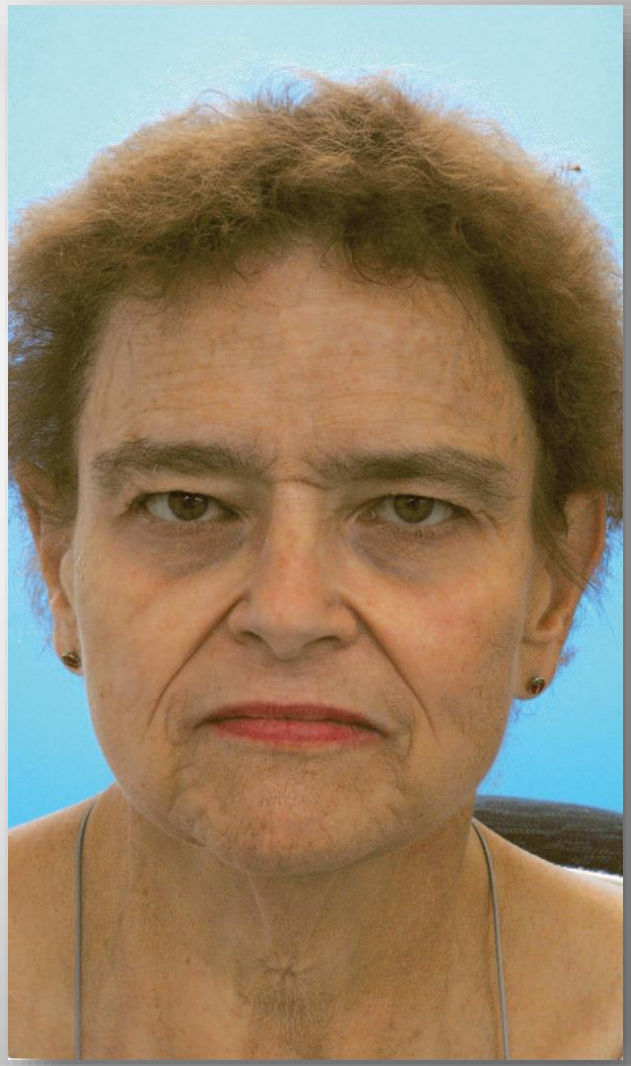
- Skin changes
  - Thickness
  - Pigment
  - Lines
- Loss of facial volume (fat)
- Muscle descent
- Changes in facial bones

Address Each Problem Area

- **Skin Changes**
  - Medical facials & peels
  - Light therapy & lasers
  - Block muscles that cause lines
  - Fill in fine lines
  - Tighten skin
- **Loss of Volume**
  - Add volume

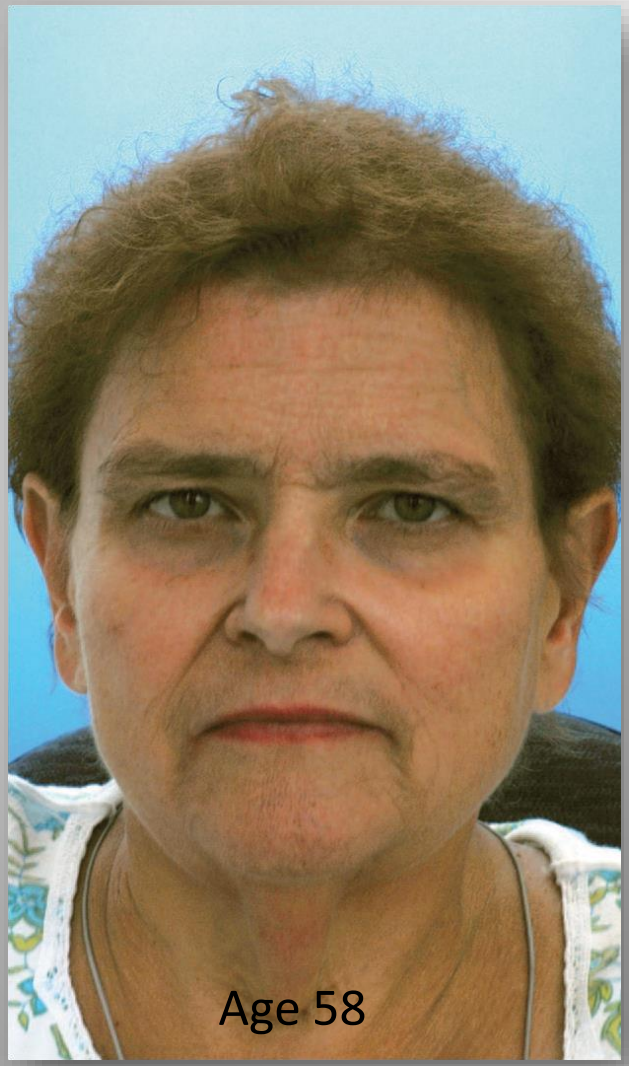
Twin Comparison: Body Mass Index

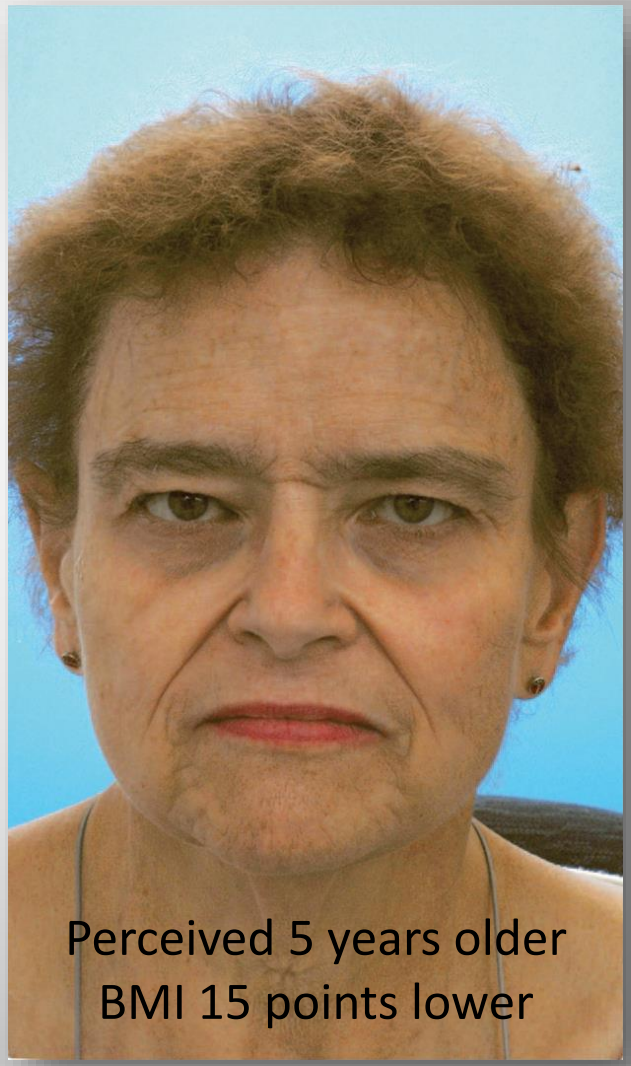




Guyuron, 2009

Twin Comparison: Body Mass Index





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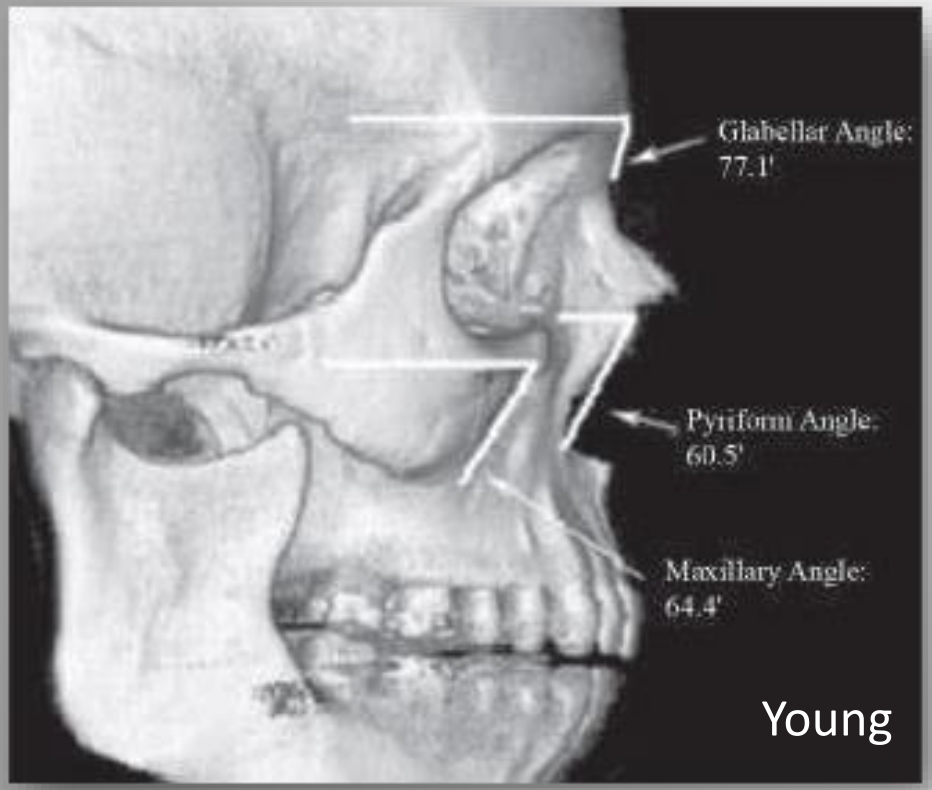
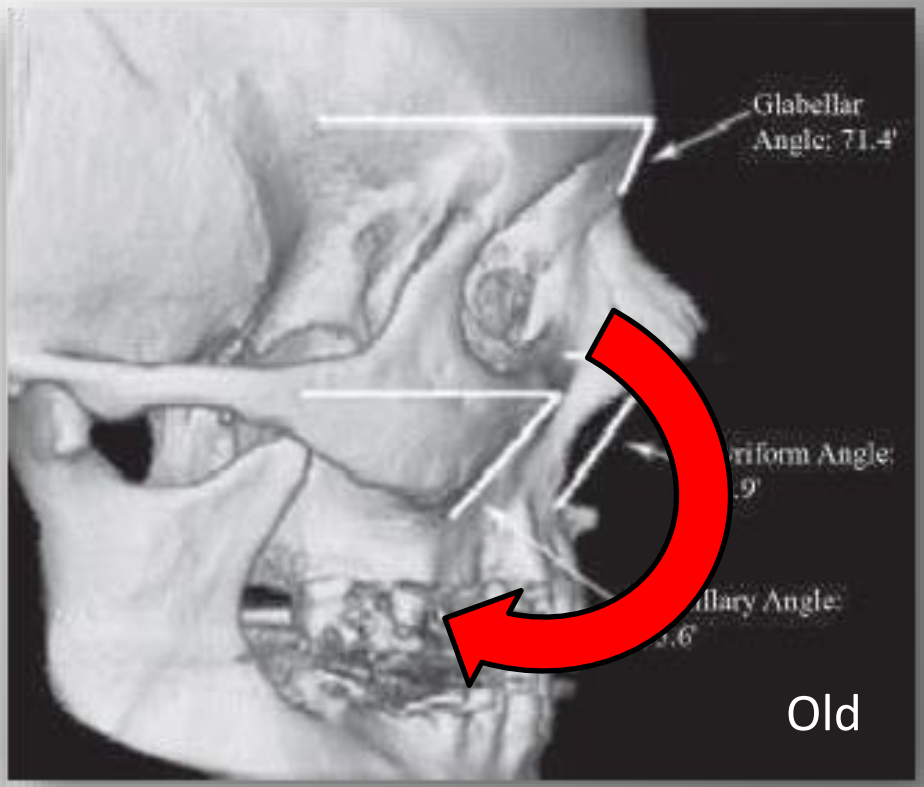
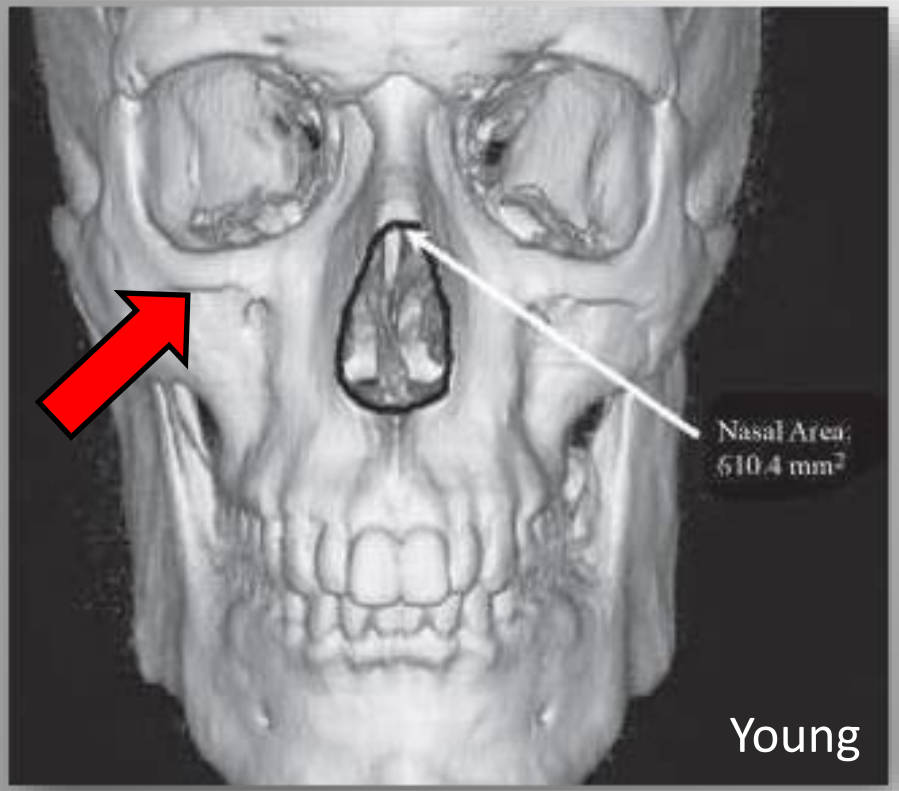
Facial Bone Changes

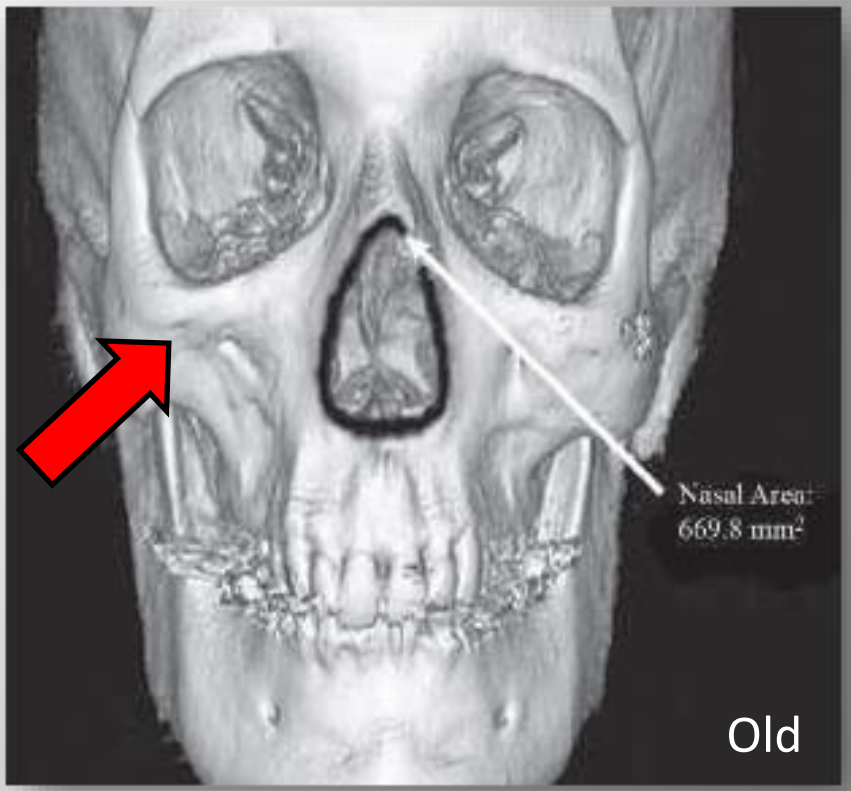




Bones in the midface and jaw become less prominent causing loss of structural support which leads to a sunken appearance

Facial Bone Changes





Bones around the eye become larger causing loss of structural support which leads to aged appearance

Injectable Options

Soft Tissue Filler Trends

COSMETIC MINIMALLY-INVASIVE PROCEDURES	2015	2014	2000	% CHANGE 2015 vs. 2014	% CHANGE 2015 vs. 2000
	2009	2008	2000	% since 2008	% since 2000
Botulinum Toxin Type A (Botox, Dysport)***	6,757,198	6,673,608	786,911	1%	759%
Cellulite treatment (Velosmooth, Endermology)	30,810	29,243	23,952	5%	29%
Chemical peel	1,310,252	1,250,059	1,149,457	5%	14%
Intense Pulsed Light (IPL) treatment	646,592	621,724	*	4%	*
Laser hair removal	1,116,708	1,112,046	735,996	0%	52%
Laser skin resurfacing	569,458	543,731	170,951	5%	233%
Ablative	159,795	152,478	*	5%	*
Non-ablative (Fraxel, etc.)	409,663	391,253	*	5%	*
Laser treatment of leg veins	207,862	207,790	245,424	0%	-15%
Microdermabrasion	800,340	881,905	868,315	-9%	-8%
Sclerotherapy	322,280	323,609	866,555	0%	-63%
Soft Tissue Fillers	2,440,724	2,295,647	652,885	6%	274%
Calcium hydroxylapatite (Radiesse)	256,256	257,953	*	-1%	*
Collagen	14,353	16,023	587,615	-10%	-98%
Porcine/bovine-based (Evolence, Zyderm, Zyplast)	14,353	16,023	*	-10%	*
Fat	70,283	67,609	65,270	4%	8%
Hyaluronic acid (Juvederm Ultra, Juvederm Ultra Plus, Perlane, Restylane, Belotero)	1,951,692	1,802,247	*	8%	*
Polylactic acid (Sculptra)	130,089	134,471	*	-3%	*
Polymethyl-methacrylate microspheres (Artefill)	18,051	17,344	*	4%	*
TOTAL COSMETIC MINIMALLY-INVASIVE PROCEDURES	14,202,224	13,939,362	5,500,446	2%	158%

The Typical Liquid Facelift

The Atypical Result

The Fillers

Filler Overload

More Options for Filler Duration

- Short-term degradable
- Long-lasting degradable
- Permanent

More Mechanisms of Action

- Volumetric
- Structural
- Fibroplastic

More Volume being Injected

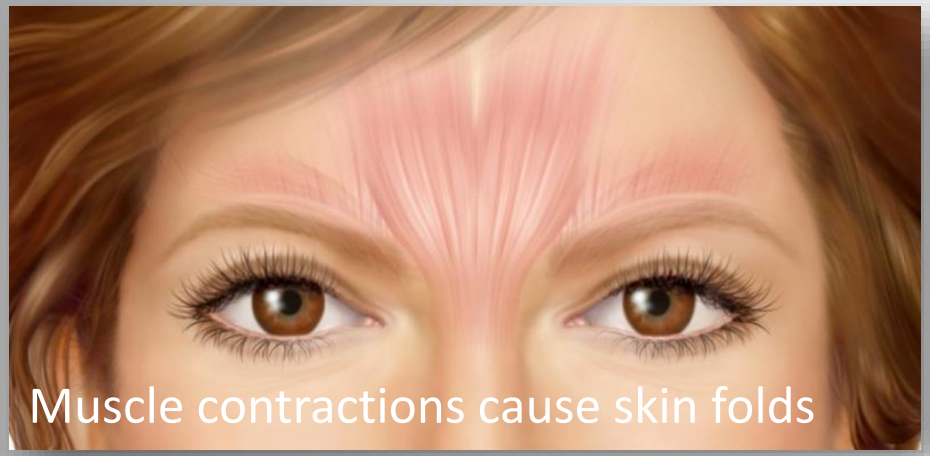
More Sites being Treated

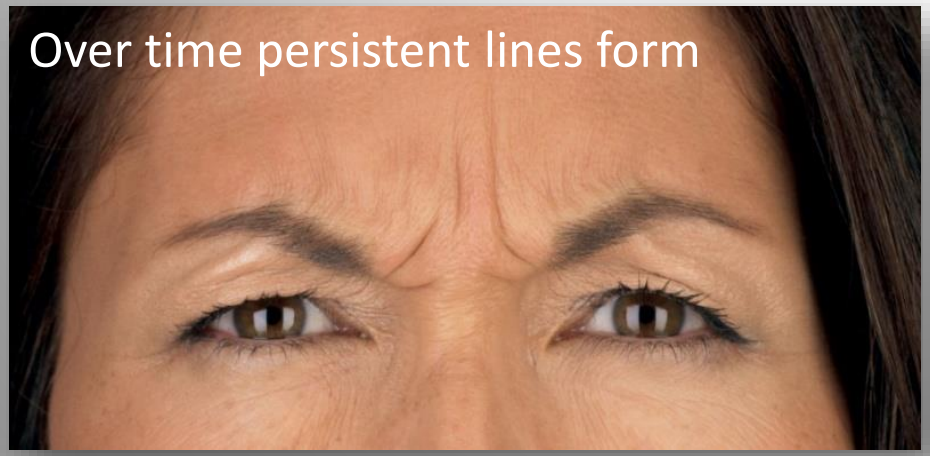
Types of Lines

Lines at Rest (Static)

Lines with Movement (Dynamic)

Cause of Lines





Perioral volume loss

Where & What to Inject

Neuromodulator (Botox, Dysport, Xeomin)

For wrinkles with movement

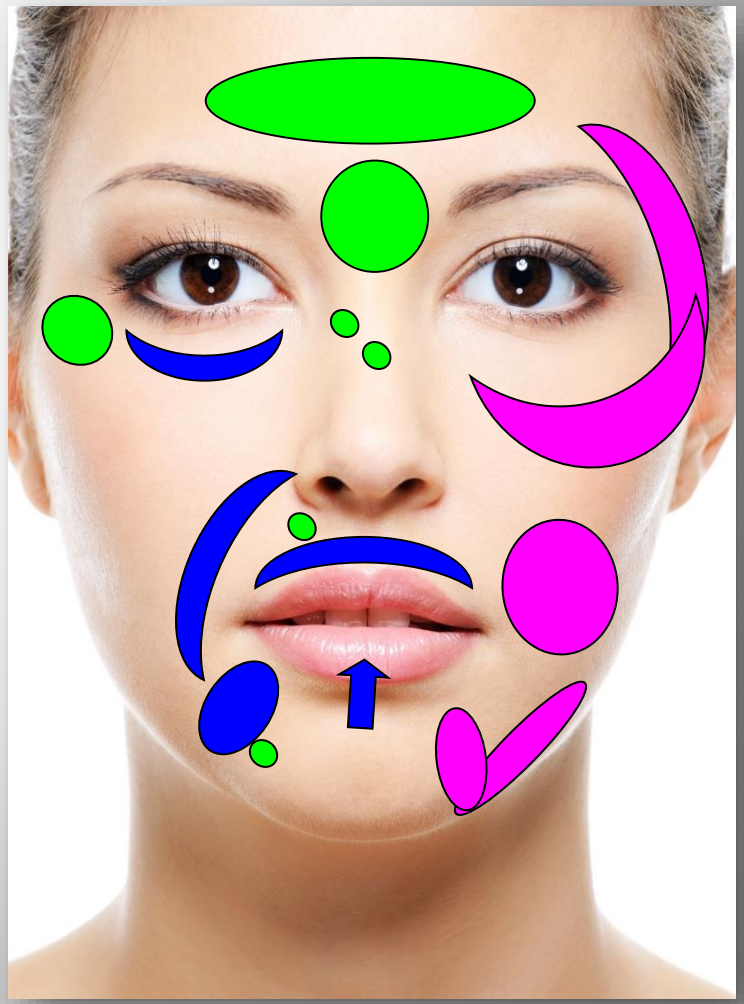
Filler (Juvederm, Restylane)

For wrinkles at rest

For small volume deficits

Stimulator (Sculptra, Bellafill)

For replacing regional volume loss



Injectable Tissue Filler Options

Silicone

Stimulators
PLLA (Sculptra)
PMM (Bellafill)

Animal Collagen
(Zyderm, Zyplasty, Evolence)

CaHA (Radiesse)

Human Collagen
(CosmoDerm, CosmoPlast, Fascian, Autologen, Cymetra, LaViv)

Hyaluronic Acids
(Juvederm & Voluma, Volbella Restylane, Belotero)
Reversible

Soft Tissue Filler Classifications

Source

- Autologous
- Biological
- Synthetic

Longevity/duration of effect

Temporary	< 6 months
Long lasting	6 to 24 months
Semi permanent	2 to 5 years
Permanent	> 5 years

Risk profile

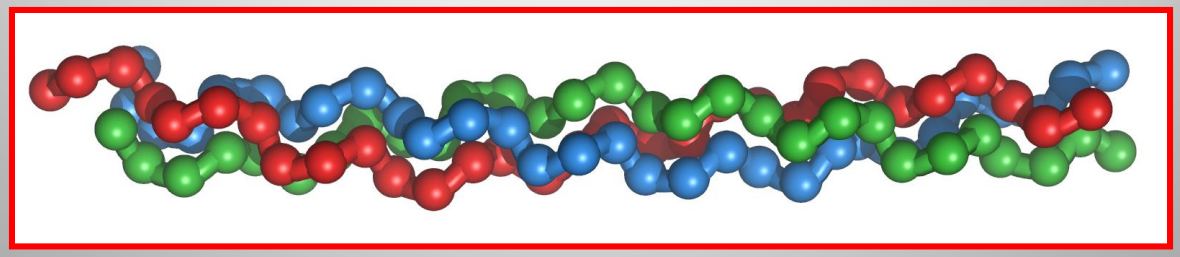
Injection expertise needed

Depth of injection

Temporary Fillers: Collagen

Bovine collagen

- First FDA approved nonautologous dermal filler (1981)
- Treatment of wrinkles, smile & frown lines, acne, postsurgical scars
- Double skin testing required (up to 3% positive)
- Allows for connective tissue ingrowth
- Excellent long-term safely profile
- Injected into dermis
- Last for 3 to 6 months



Collagen 1980s

Zyderm 1 35 mg/mL collagen + 0.3% lidocaine

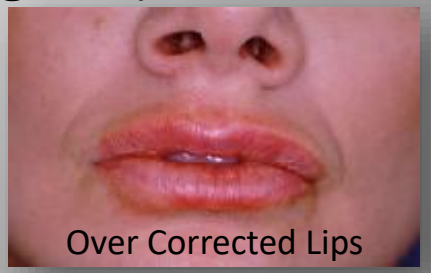
- Injected into superficial papillary dermis
- 100% overcorrection recommended because of water loss

Zyderm 2 65 mg/mL collagen + 0.3% lidocaine

- Injected into mid-dermis
- 50% overcorrection recommended

Zyplast 35 mg/mL collagen + 0.3% lidocaine

- Longer-lasting due to cross linking (less immunogenic)
- Injected into deep dermis
- No overcorrection


Over Corrected Lips

Collagen New Millennium

CosmoDerm Human-derived collagen equivalents of Zyderm

CosmoPlast Human-derived collagen equivalents of Zyplast

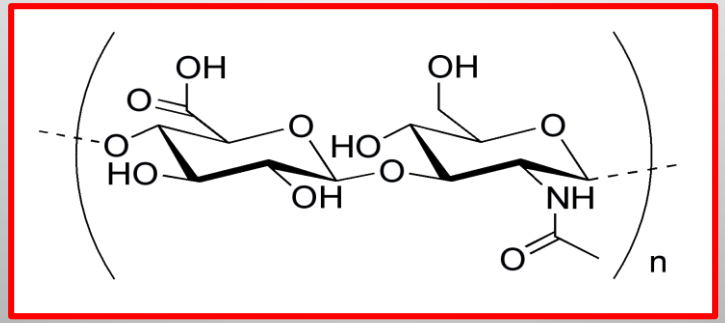
- FDA approved 2003
- No skin testing

Evolence 35-mg/mL type I collagen

- FDA approved 2008
- Cross-linked porcine collagen (skin testing not required)
- No overcorrection, lasts up to 1 yr
- Correction of moderate to deep wrinkles & folds (NLF)
- Not into lips (nodule formation)
- Discontinued late 2009 (tough market)

Temporary Fillers: Hyaluronic Acid

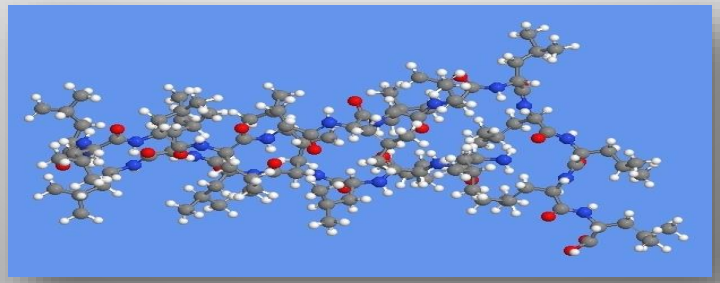
- Glycosaminoglycan biopolymer
- Found in all connective tissue
- Chemically the same for all species
  - Low risk for allergic reactions
  - Skin testing is not required
- Hydrophilic - provides matrix to retain dermal moisture
  - One gram of HA can bind up to 6 L of water
- Hyaluronic gels (Hylans) = Cross-linked to increase longevity



Hyaluronic Acid Properties

Unique to hylan fillers

- Dynamic viscosity
  - Decreasing viscosity as shear rate increases
  - Upon injection hylans pass through needles more easily
  - When force removed, viscosity increases, gel thickens to minimize migration
- Isovolemic degradation
  - As it degrades, the remaining HA bind more water
  - Overall volume remains the same
  - Maintain 95% of initial filling volume until all is resorbed



Hyaluronic Acid Products

Animal Based HAs from dermis of rooster combs

- **Hylaform**
  - First HA available (but approved 2004)
  - Mid to deep dermis for moderate to severe wrinkles & folds (NLF)
- **Hylaform Plus**
  - Larger particle size (750 vs 500 mm) & greater gel hardness
  - Greater ability to deform surrounding tissues to correct defects
  - Intended for deeper injections

Hyaluronic Acid Products

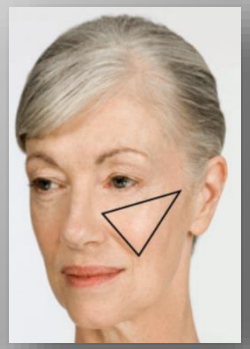
Non-Animal Based HAs from *Strep equi*

- **Restylane**
  - First FDA approved filler (2003)
  - Correction of moderate to severe wrinkles and folds (NLF)
  - 20 mg/mL, uniform 400 mm particles,1% cross-linked
  - 6 month duration
  - More viscous & less elastic than Hylaform
- **Restylane Silk** for lips & lip lines
- **Restylane Lyft** for deeper folds

- **Belotero Balance** for perioral & NLF, fine lines

Hyaluronic Acid Products

- **Juvederm Ultra** (2006)
  - Mid to deep dermis for moderate to severe wrinkles & folds (NLF)
  - Higher HA concentration (24 mg/mL) than Restylane
  - More crosslinking than Restylane to increase longevity
  - Last up to 12 months
- **Juvederm Ultra Plus**
  - Larger particle size & more cross-linking
  - Thicker gel for volumizing deeper injections
- **Juvederm "XC"** includes 0.3% lidocaine
- **Voluma** (2013)
  - More "lift" for cheek elevation
  - Lasts up to 18 months



Does HA Stimulate Collagen?

Fillers and Neocollagenesis

JEAN D. A. CARRUTHERS, MD, FRCSC, FRCOPHTH,* J. ALASTAIR CARRUTHERS, MBBS, MRCP, FRCPC,† AND SHANNON HUMPHREY, MD, FRCPC, FAAD‡

HA fillers show increased collagen around injection site for at least 3 months

HA Filler Physical Properties

	Hylaform	*Hylaform Plus*	*Prevelle*	*Restylane*	*Perlane*	*Juvederm 30 HV*
Total HA concentration (mg/mL)	5.5	5.5	5.5	20	20	24
Gel-to-fluid ratio	98:2	98:2	98:2	75:25	75:25	60:40
HA gel concentration (mg/mL)	5.4	5.4	5.4	15.0	15.0	14.4
Degree of HA modification (%)	23	23	23	3	3	10
Percentage cross-linked HA	12	12	12	1.2	1.4	2
Dilution durability/percentage swelling	<25	<25	<25	50	50	300
G′ modulus (Pa)	140–220	140–220	230–260	660	588	105
Average particle size (μm)	500	700	350	300	650	300

HA products are NOT interchangeable

Filler Rheology

Basics of Dermal Filler Rheology

Sébastien Pierre, PhD,* Steven Liew, MD,† and Aude Bernardin, PhD*

Filler	G′ (Pa)	G″ (Pa)	Tan δ	Compression (gmf)
Juvéderm Ultra XC	207	80	0.39	96
Juvéderm Ultra Plus XC	263	79	0.30	112
Juvéderm Voluma XC	398	41	0.10	40
Juvéderm Volift with lidocaine†	340	46	0.14	30
Juvéderm Volbella with lidocaine†	271	39	0.14	19
Restylane-L	864	185	0.21	29
Perlane-L	977	198	0.20	32
Belotero Balance	128	82	0.64	69

Filler Rheology

G' = Elastic behavior (modulus)
How much it can recover after a stress force

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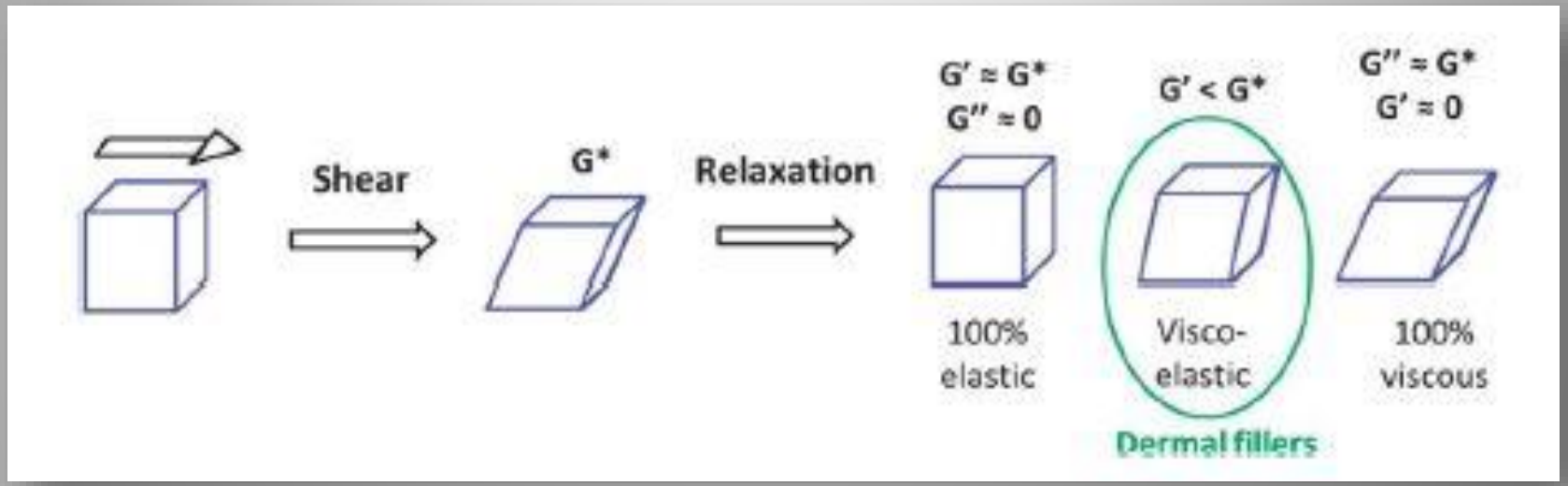
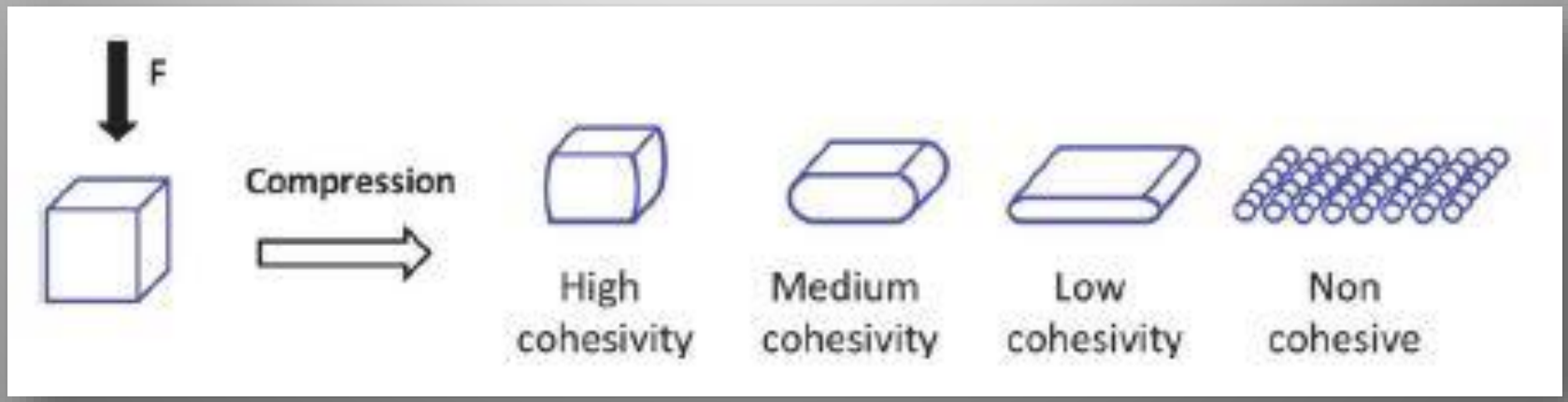
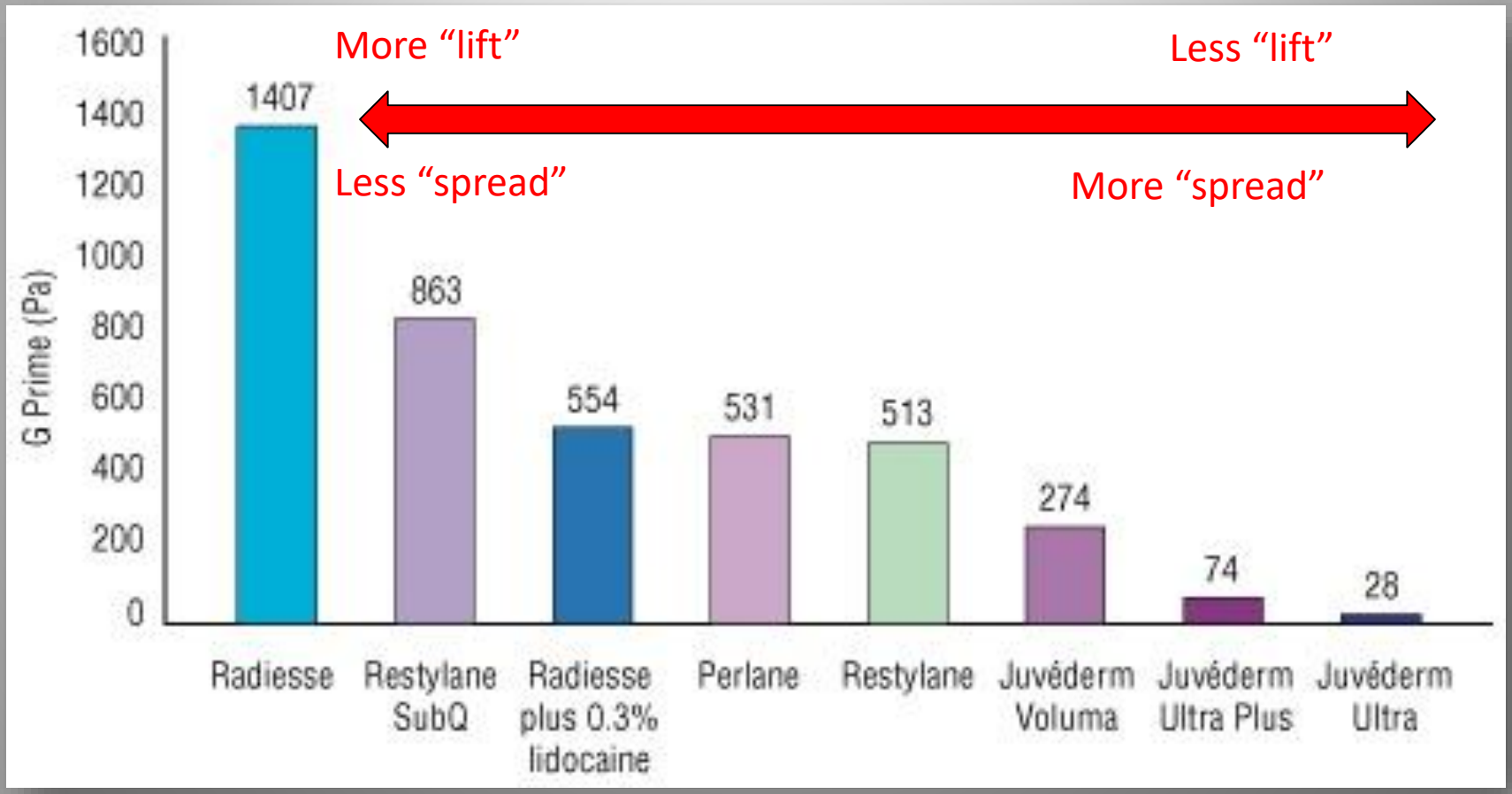
Filler Rheology





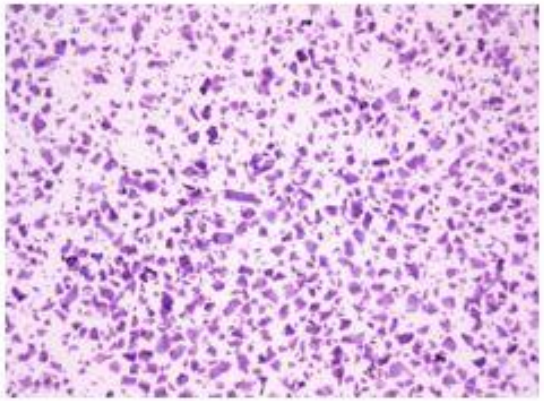
Elastic Modulus* (G prime)



*Mathematical description of product’s tendency to be deformed elastically
May not match clinical results

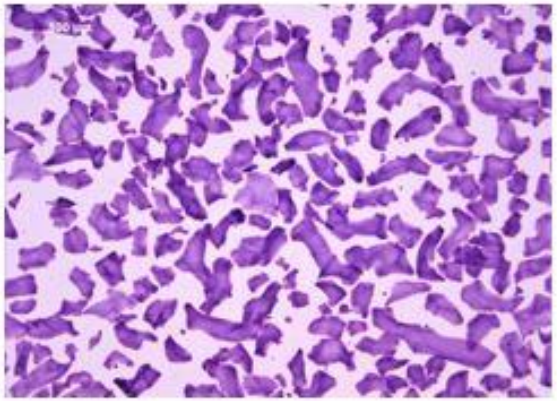
Restylane Product Particle Size

Silk



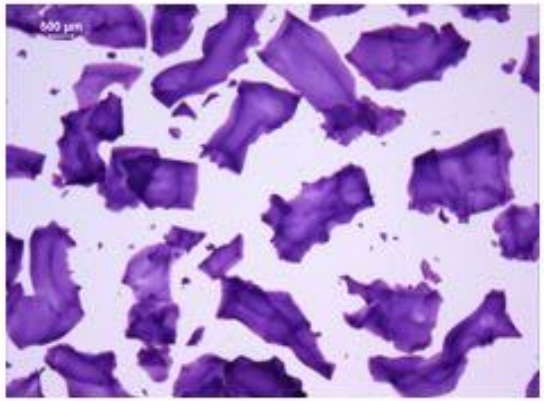
Small Particle HA
Range of 50–220 µm*

Restylane



Small Gel Particle HA
Range of 330–430 µm*

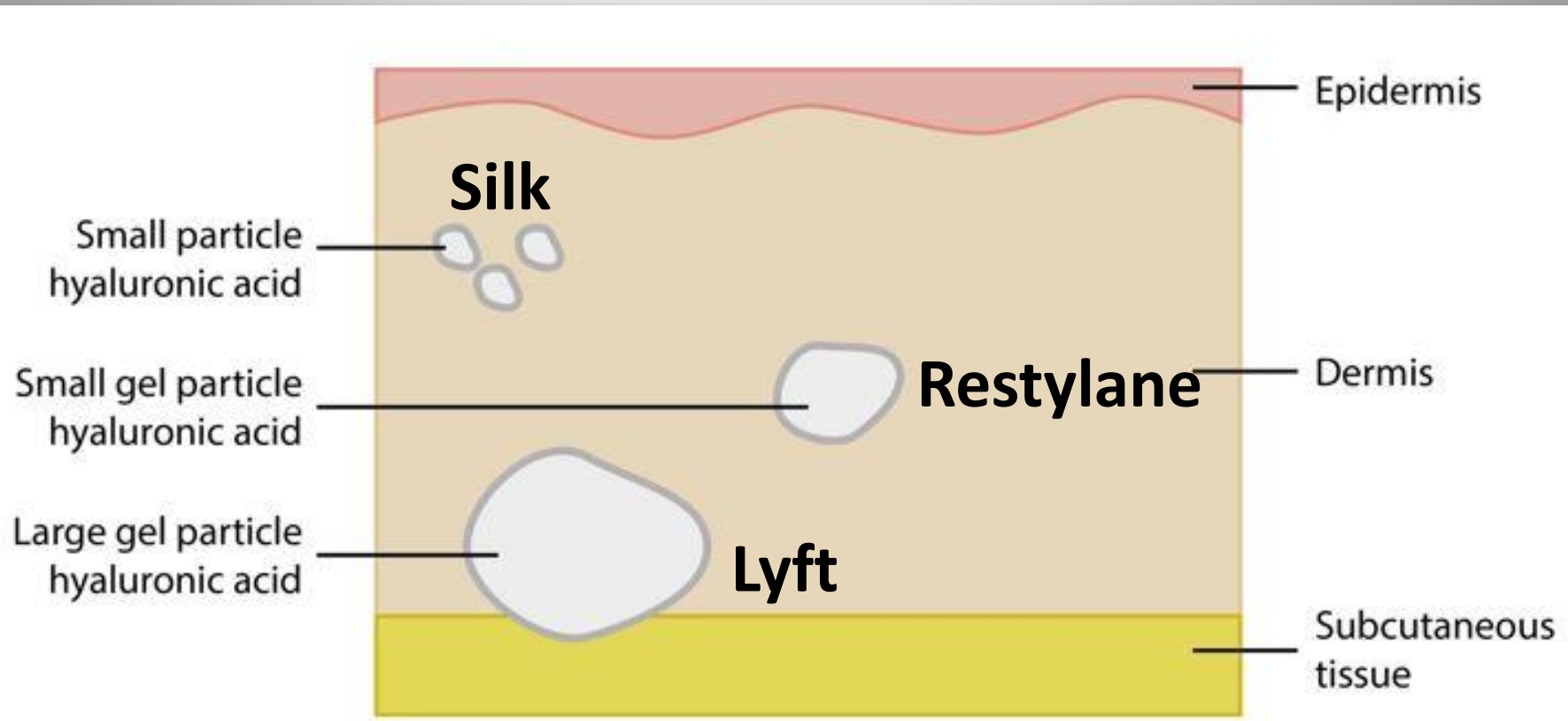
Lyft



Large Gel Particle HA
Range of 750–1000 µm*

All 3 have 20 mg HA per mL
Particle size is different

Particle Size & Injection Depth



Rheology & Filler Choice

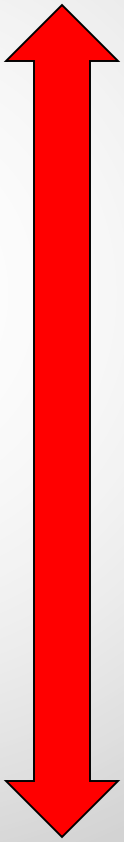
- Midface
  - Use higher G' products
  - Lift & fill
- Fine lines & wrinkles
  - Use low-moderate G' products
  - Easy to mold
  - Less visible

Water Absorption

Prevelle Silk

Restylane and Lyft

Juvéderm Ultra Plus



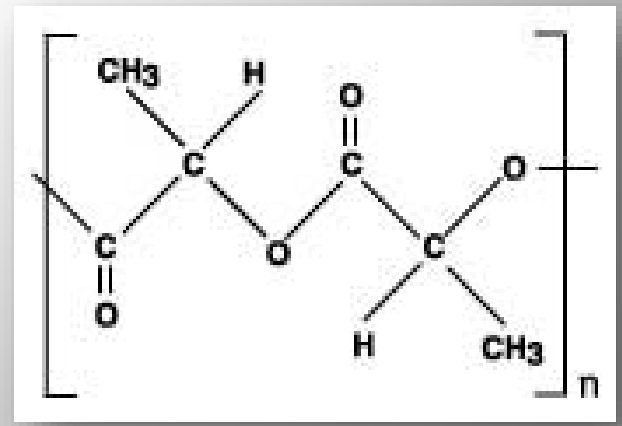
Less Swelling

More Swelling

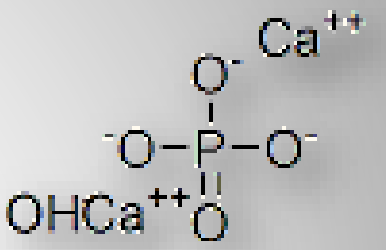
Long Lasting Fillers: PLLA

Poly L Lactic Acid

- Biodegradable, nontoxic, synthetic, inactive material from corn starch
- Used in sutures, stents, other biomedical implants
- Growth of type I collagen into injection sites
- Metabolized to CO_2 & glucose
- **Sculptra** (2004) HIV-related facial lipoatrophy then cosmetic indications
  - Up to 2 year duration
  - Provides true volumization
  - Not an instant results filler
  - Requires temporary overcorrection
  - Reassess at 4-6 weeks



Semipermanent Fillers: CaHA



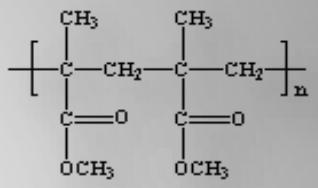
Calcium Hydroxylapatite

- Mineral component of bone
- Non immunogenic & biocompatible
- Scaffold for collagen in-growth
- Dental, orthopedic, urologic, & vocal cord applications
- **Radiesse** (2006) HIV facial lipoatrophy & cosmetic indications
  - Spheres (24 - 45 µm) suspended in carboxymethylcellulose gel
  - Highly viscous
  - Predisposed to nodule formation, especially in lips
  - 9 to 18 month duration but may last 2 to 5 years

Permanent Fillers

Autologous Fat - The original filler

Silicone - Controversial


PMMA

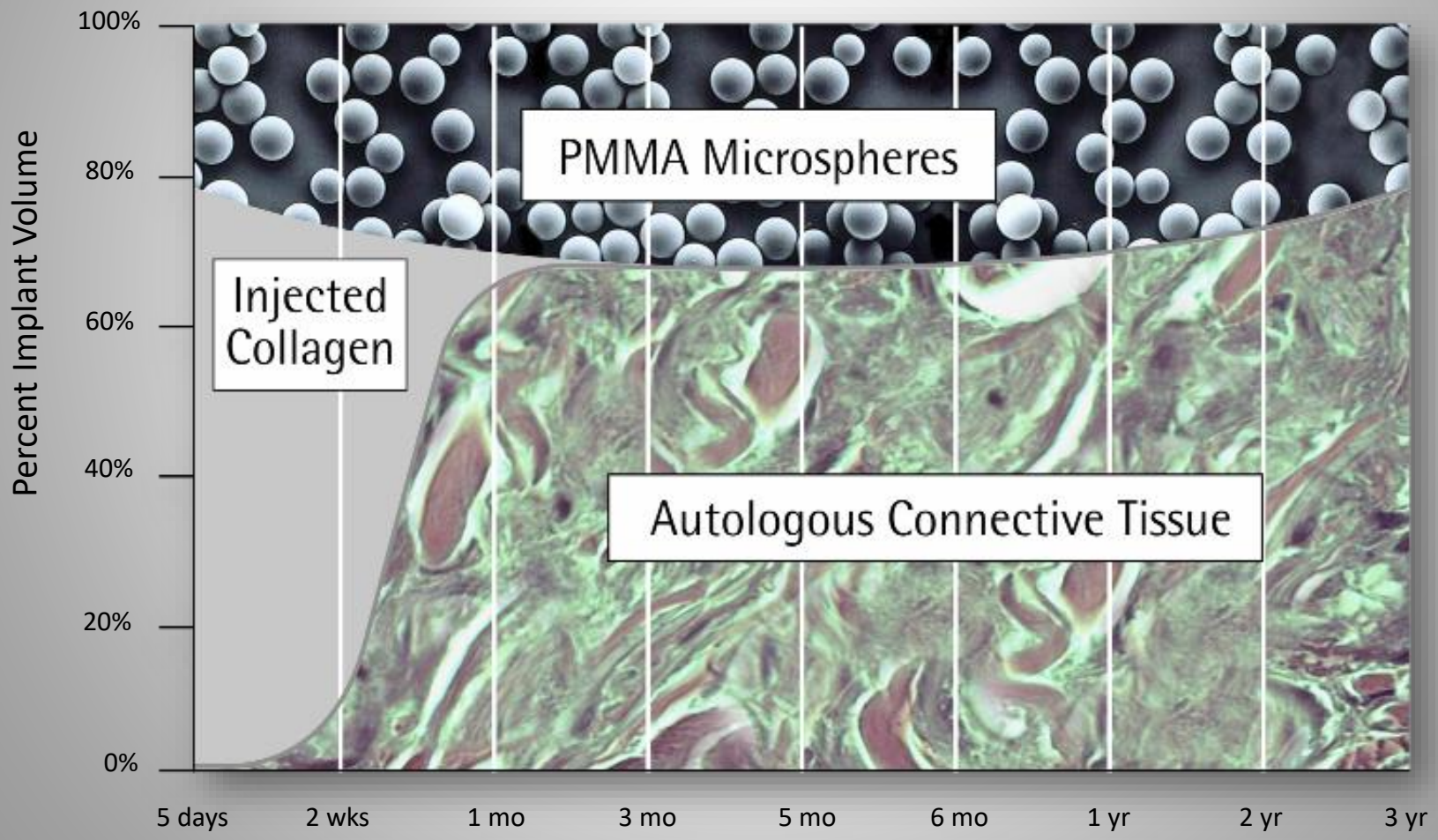
Polymethylmethacrylate (PMMA, Plexiglas, Lucite, acrylic glass)

- Used in bone cement, lenses, dental work, pacemakers
- **Bellafill** (2015, **Artefill** 2003) correction of nasolabial folds (**Artecoll** in Europe)
  - Microspheres (30 - 42 mm) in 3.5% bovine collagen + 0.3% lidocaine
  - Skin test needed
  - Collagen stimulation & ingrowth as bovine collagen dissolves
  - Off the market in 2008 (Artes out of business), back in 2009

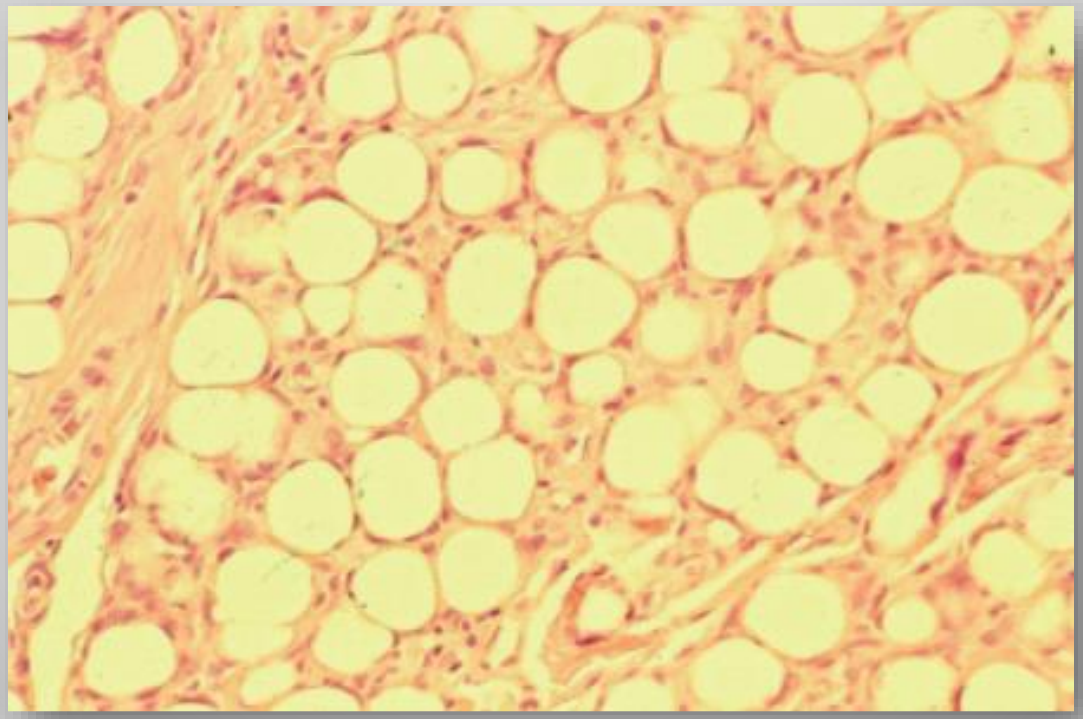
Aquamid (World wide use, not FDA approved)

- Acrylic polymer hydrogel

Scaffold for Collagen Deposition

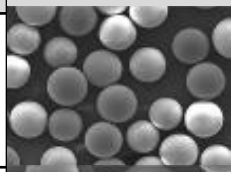
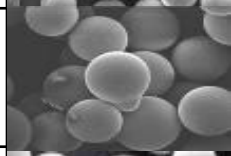
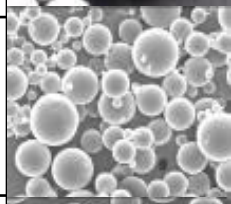
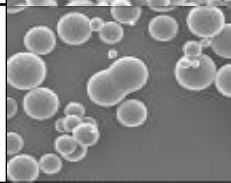


PMMA Encapsulation after 3 Months



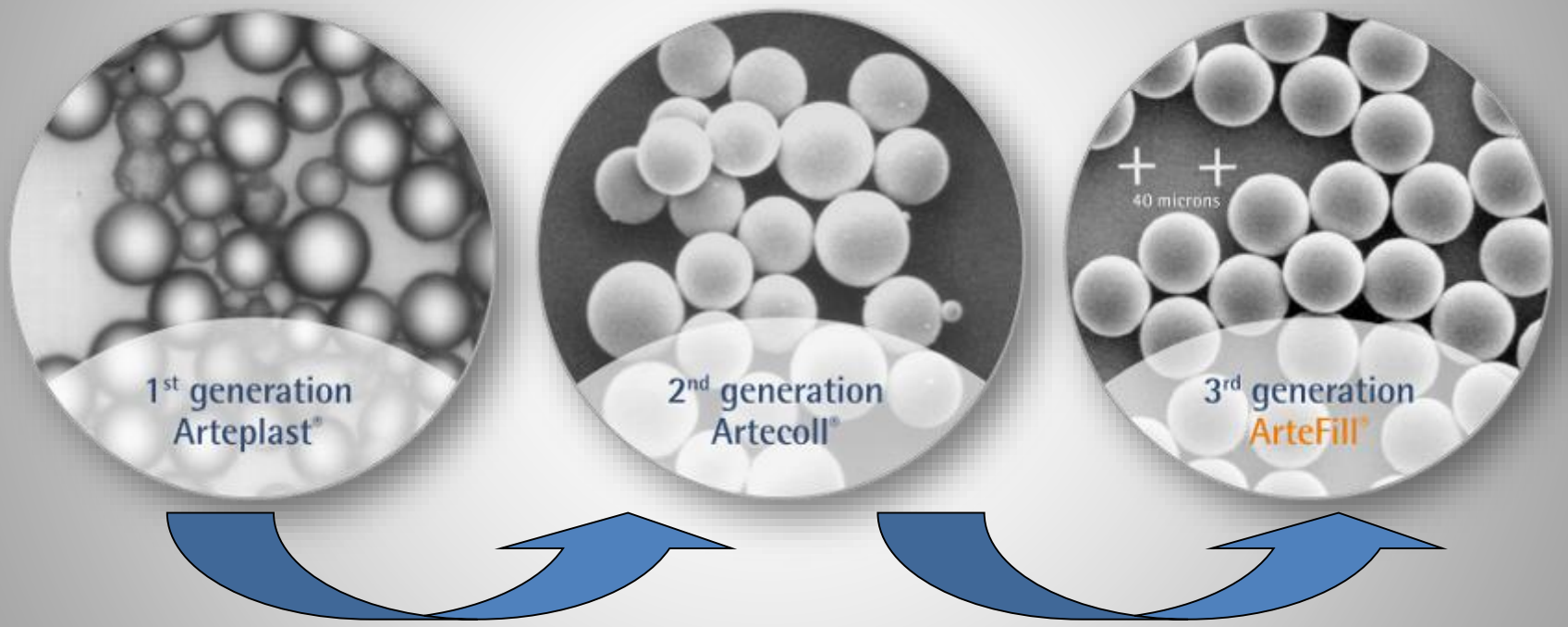
Multiple fibroblasts & connective tissue encapsulation of individual microspheres

PMMA Variability

Product	Country of Origin	SEM Analysis (Particle shape, surface finish, size, gross size distribution, and anomalies)	SEM Image
Artefill 2007	**USA**	▪ Size: 30 to 50 microns, with negligible small sizes. ▪ Shape: Smooth surfaced microspheres with scant if any sediment. ▪ The only FDA approved PMMA-enhanced dermal filler	
Artecoll 2005	**Canada**	▪ Size: 30 to 50 microns, with negligible small sizes. ▪ Shape: Smooth surfaced microspheres with slight surface irregularity, scant sediment.	
Artecoll 2001	**Europe**	▪ Size: 32 to 40 microns, but with larger variation in particle sizes ▪ Shape: presence of nanoparticles on the surface of microspheres. ▪ There are sub-20 micron particles and some sub 5 micron particles, some sediment.	
Metacrill 2006	**Brazil**	▪ Size: 0.2 to 60 microns. Many sub-20 micron particles, and many are sub-5 micron. ▪ Shape: Many irregular shapes, some non spherical, jagged edges, poor surface.	
NewPlastic 2006	**Brazil**	▪ Size: 0.2 to 70 microns. Some large spheres > 70 microns and some very small. ▪ Shape: Some are non spherical, and conjoined, many small spheres and particles.	

PMMA Production Evolution

Arteplast | **Artecoll** | **Artefill & Belafill**



Contaminant Elimination

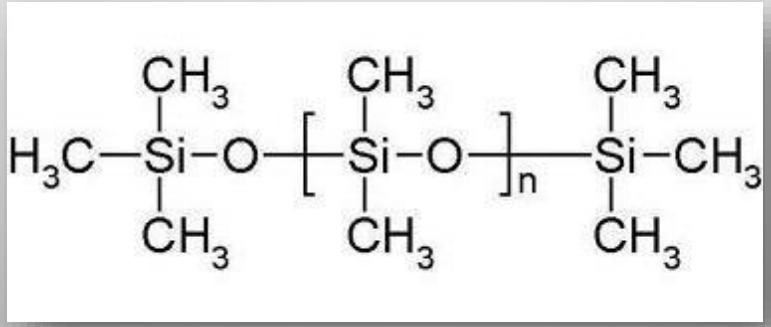
Production control to insure MS are round & smooth

Uniform particle size (30 – 50 µm)

<1% are <20 µm per FDA

Silicone

- 1992: FDA bans liquid injectable silicone
- 1994 & 1997: FDA approves AdatoSil (Adaptosil) 5000 & Silikon 1000 (highly purified silicone) for retinal detachment
- 1997: FDA Modernization Act allows off label use of devices
- Filler indication is strictly off-label
- Liability carriers have regulations on liquid injectable silicone



Silicone

Largest report of Silikon 1000

- 916 patients over 6 years
- 5246 treatments during 3307 visits
  - 3.5 visits per patient
  - 1.6 treatments per visit
- Adverse events
  - Overcorrection in 11 patients (1%)
  - Retrospective chart review limitations

Hevia 2009

Silicone for Acne Scars

Barnett 2010

Silicone for HIV Facial Atrophy

Barnett 2010

Silicone Summary

- FDA studies underway to assess safety & efficacy
- Silicone injections remain controversial
- Inherently unpredictable, adverse events

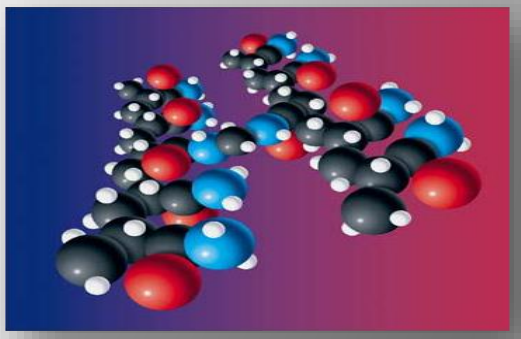
  versus

- Safe & effective, giving superior aesthetic results if:
  - Use highly purified silicone
  - Microdroplet technique (0.01 cc into subdermal plane 2-4 mm intervals)
  - Small volumes ($\leq$ 0.5 cc for smaller defects, $\leq$ 2 cc for facial lipoatrophy)
  - Limit injections to once monthly (allow fibroplasia augmentation)
- May be ideal filler if injected correctly
- Complications similar to other FDA approved fillers

Aquamid

2.5% Cross-linked polyacrylamide (PAAG)

- Homogeneous gel, no microparticles
- No foreign body reaction to achieve augmentation
- Permanent results (up to 11 years)
- Approved in Europe (2001)
- NLF, lips, cheeks, nose, facial lipoatrophy



Aquamid

Adverse reactions following injection with a permanent facial filler polyacrylamide hydrogel (Aquamid): causes and treatment

- Prospective study of 40,000 case reports between 2003
- 55 were reported to have experienced adverse events (AE)
  - AEs occurred mainly in lips and nasolabial folds
  - 55 patients, with 51 requiring treatment
  - The time from last injection to AE: 2 to 364 days (median of 12 days)
  - High dose broad-spectrum antibiotic effective for a short time
  - Steroids & NSAIDS NSAIDs) aggravated symptoms & prolong treatment time
- Conclusions: Nodules or swellings later than 1 week and less than 1 year should be treated immediately
  - Broad-spectrum antibiotic (quinolone) in high dosage
  - Steroids & NSAIDs contraindicated

Christensen 2006

Aquamid Product Guidelines

Tingling, redness, swelling or other changes in the first weeks are usually sign of infection

In the event of complications, suspect an infection - these are NOT an allergic reaction

Never corticosteroids

- Complications, such as swelling, should NEVER be treated with corticosteroids or NSAIDs as they are absolutely contraindicated because they prolong recovery time

Treat with antibiotics (high-dose & broad spectrum)

- Clarithromycin 500 mg + Moxifloxazin 400 mg BID, at least 10-14 days
- If no reduction after 3 days, change to Clindamycin 600 mg + Tetracyclin 500 mg BID
  - This combination may act against bacteria resistant to Clarithromycin + Moxifloxacin

Prophylactic antibiotics

- If you choose to use a prophylactic treatment, the following is recommended: Azithromycin 500 mg + Moxifloxacin 400 mg 2 - 6 hours prior to injection

Aquamid Abscess

Acute swelling 3 years after Aquamid injection

Recurrent abscess

Platelet Rich Plasma (PRP)

PRP: What is it?

Autologous blood plasma enriched with platelets

Degranulation release cytokines & growth factors

- Platelet-derived growth factor
- Transforming growth factor beta
- Fibroblast growth factor
- Insulin-like growth factors 1 & 2
- Vascular endothelial growth factor
- Epidermal growth factor
- Interleukin 8
- Keratinocyte growth factor
- Connective tissue growth factor

PRP Production

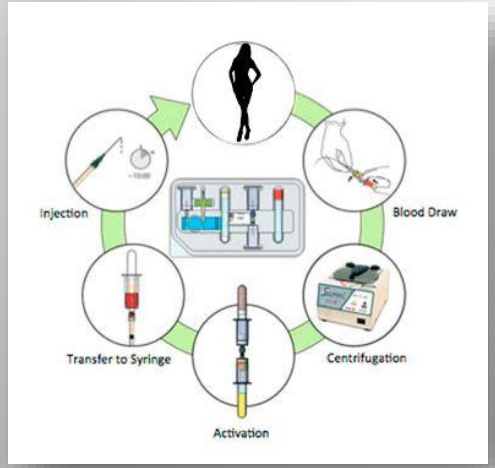
- Collection of anticogulated whole blood
- Two-stage centrifugation
- PRP separated from platelet poor plasma & RBCs
- 5-fold increase in platelet concentration
- Broad variability in production techniques

Selphyl

PRP & Ca^{++} to activate fibrinogen to fibrin

Results in a gel matrix

Limited clinical data



SELPHYL®
Platelet Rich Fibrin Matrix System

Vampire Lift: PRP & HA Filler

PRP injected with Restylane or Juvederm

Proprietary methods

No clinical data

PRP in Facial Aesthetics

- 15 adults: Single PRFM (Selphyl) injection for deep nasolabial folds
- Wrinkle Assessment Scale (WAS 1-5)
  - Reduction of 1.1 ± 0.7 after 12 weeks
- No complications
- Holds potential for dermal augmentation

Anthony P Sclafani MD, 2010

PRP in Facial Aesthetics Follow Up

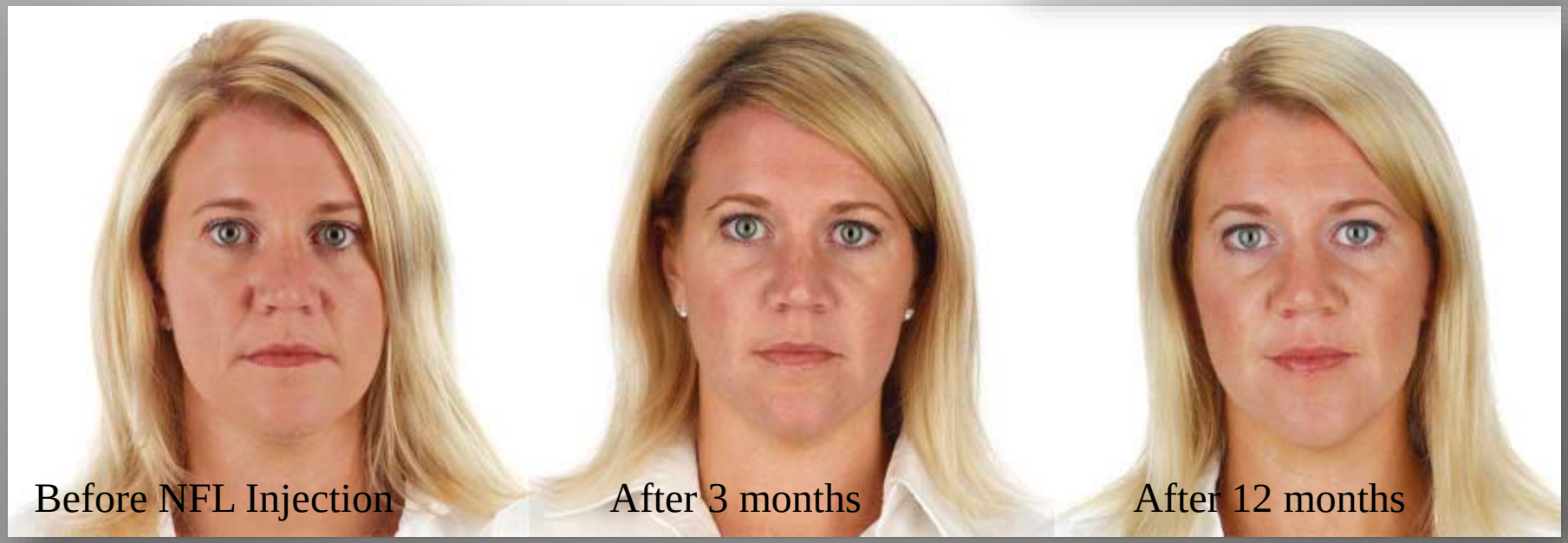
- 50 adults with mean 10 month follow up
- NLFs, acne scars, rhytides, volume loss
- Average 1.6 treatments (Range 1-5)
- “Most patients were satisfied”

ORIGINAL ARTICLE

ONLINE FIRST

Safety, Efficacy, and Utility of Platelet-Rich Fibrin Matrix in Facial Plastic Surgery

Anthony P. Sclafani, MD



No Advantage in Fat Grafting for Facial Wasting

Double-Blind Clinical Trial to Compare Autologous Fat Grafts versus Autologous Fat Grafts with PDGF: No Effect of PDGF

Joan Fontdevila, M.D., Ph.D.
Eva Guisantes, M.D., Ph.D.
Esteban Martínez, M.D., Ph.D.
Eduard Prades, M.D.
Juan Berenguer, M.D.

Barcelona, Spain

Background: This work evaluates the effect of adding platelet-derived growth factor to autologous adipose tissue grafts in the treatment of human immunodeficiency virus facial lipoatrophy by means of objective measurements.
Methods: This is a randomized clinical trial conducted at the Hospital Clinic of Barcelona. Patients with facial human immunodeficiency virus atrophy were randomized into two groups, one treated with autologous fat injection (group A), and another treated with autologous fat injection with plasma rich in growth factors (group B). Before the treatment, structural changes were identified in facial soft tissue by means of computed tomography, and clinical changes were also assessed by means of photographic records. Posttreatment assessments were repeated after 2 and 12 months to compare the results. Posttreatment complications were recorded.
Results: Forty-nine patients (33 men and 16 women), with a mean age of 46 years, participated in the study. In both groups, there was a statistically significant average increase of volume in the facial area measured by computed tomography between the baseline and the 2- and 12-month posttreatment assessments. All cases showed an improvement of the clinical facial atrophy grade after treatment, which was statistically significant. This improvement was related to a statistically significant fat volume increase measured by means of computed tomography. There was no difference in the volume gain between both groups. No major complications were observed.
Conclusions: Fat grafting is a safe, effective, and durable treatment for human immunodeficiency virus facial atrophy. The results of this study show that it is not necessary to add plasma rich in growth factors to the adipose tissue graft to get a better result. (*Plast. Reconstr. Surg.* 134: 219e, 2014.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

> 2-Fold Volume Retention in Facial Fat Grafting

TISSUE ENGINEERING: Part C
Volume 15, Number 00, 2009

DOI: 10.1089/ten.tec.2008.0518

Application of Platelet-Rich Plasma in Plastic Surgery: Clinical and *In Vitro* Evaluation

Valerio Cervelli, M.D.,[1] Pietro Gentile, M.D.,[1] Maria Giovanna Scioli, B.D.,[2] Monica Grimaldi, M.D.,[1] Carlo Umberto Casciani, M.D.,[3] Luigi Giusto Spagnoli, M.D.,[2] and Augusto Orlandi, M.D.[2]

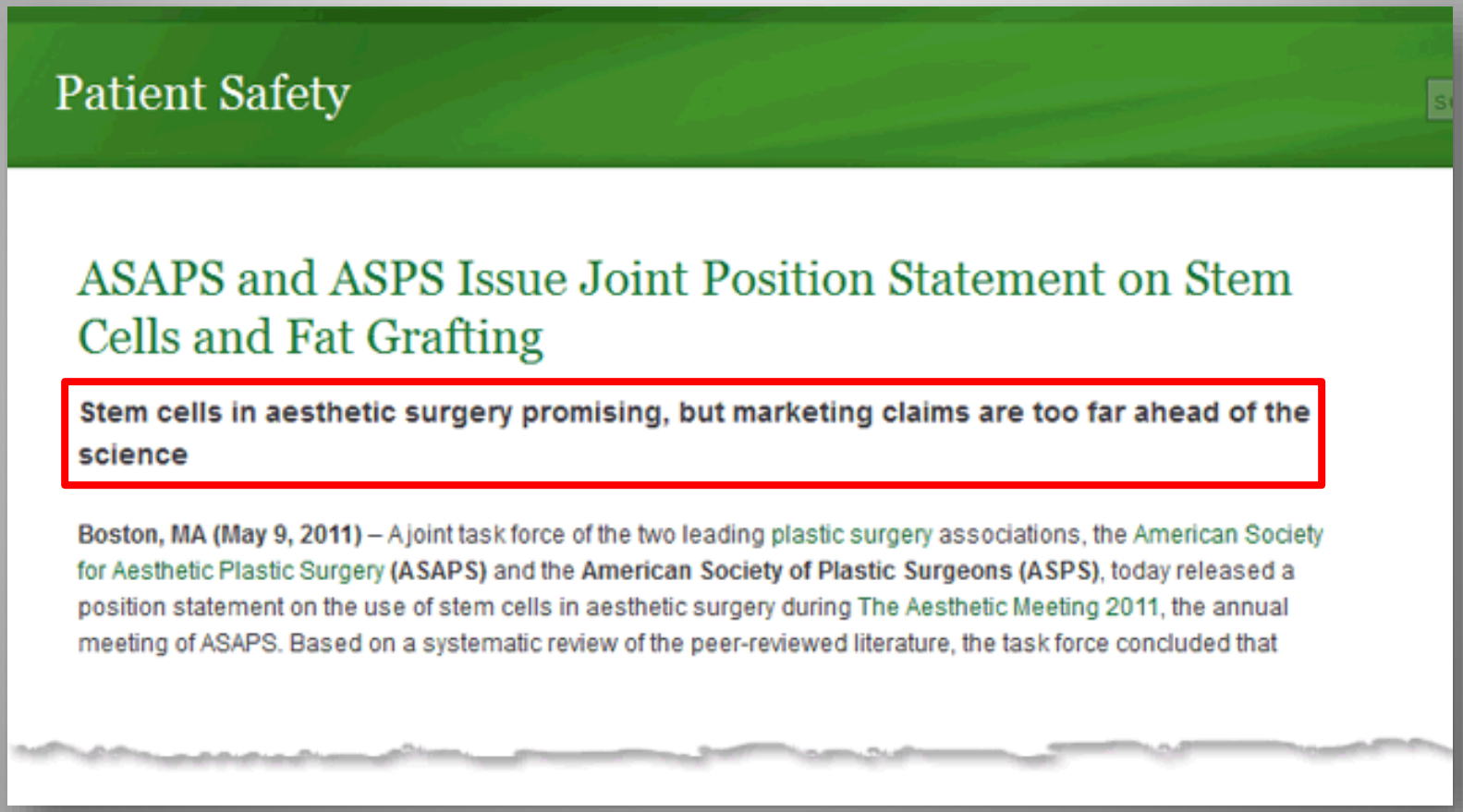
The clinical use of platelet-rich plasma (PRP) for a wide variety of application has been reportedly employed most prevalently in problematic wounds, maxillofacial and hemi-facial atrophy, Romberg Syndrome, and diabetic foot ulcers. To our knowledge, PRP has never been described in the enhancement of fat grafting during tissue-engineering application *in vivo*. The authors describe the preparation of PRP and its use in a series of 43 patients who underwent plastic, reconstructive, and maxillofacial surgery for chronic lower extremity ulcers ($n = 18$) and multiple facial applications ($n = 25$). PRP mixed with fat grafting was used in 76% patients affected by multiple facial diseases and in 88.9% patients affected by lower extremity ulcers. PRP injection alone was used in the remaining patients. The authors observed that after a 7.1-week and 9.7-week (average) course of twice-daily wound treatment with PRP suspended on a collagen base, 61.1% and 88.9% of chronic lower extremity ulcers underwent to 100% reepithelization compared with 40% and 60% of controls ($n = 10$) treated with hyaluronic acid and collagen medication. In patients treated with reconstructing three-dimensional projection of face by fat grafting and PRP, we observed a 70% maintenance of contour restoring and three-dimensional volume after 1 year compared to only 31% of controls ($n = 10$) treated with fat grafting alone. *In vitro*, PRP induced a significant increase in the number of adipose-tissue-derived stem cells compared to control cultures. These results documented that PRP accelerates chronic skin ulcer reepithelization and improves maintenance and function of fat graft in patients who underwent plastic reconstructive surgery, possibly by stimulating adipose-tissue-derived stem cell proliferation.

PRP Clinical Conclusions

- May enhance tissue graft survival
- May improve selected wound healing
- No evidence of enhanced injury repair
- Limited support for facial aesthetic uses

- Variability in PRP activation & processing limits reproducibility of results

Stem Cell Fillers



Patient Safety

ASAPS and ASPS Issue Joint Position Statement on Stem Cells and Fat Grafting

Stem cells in aesthetic surgery promising, but marketing claims are too far ahead of the science

Boston, MA (May 9, 2011) – A joint task force of the two leading plastic surgery associations, the American Society for Aesthetic Plastic Surgery **(ASAPS)** and the **American Society of Plastic Surgeons (ASPS)**, today released a position statement on the use of stem cells in aesthetic surgery during The Aesthetic Meeting 2011, the annual meeting of ASAPS. Based on a systematic review of the peer-reviewed literature, the task force concluded that

NO clinical studies support stem cell use in plastic surgery

Technique

Factors in Unfavorable Outcomes

- Patient selection
- Undertreatment
- Anatomic site
- Product selection
- Technique
- Judgment (overfill/under correction)
- Patient expectations
- Tissue damage

Assessment Scale to Set Expectation

Wrinkle Scale

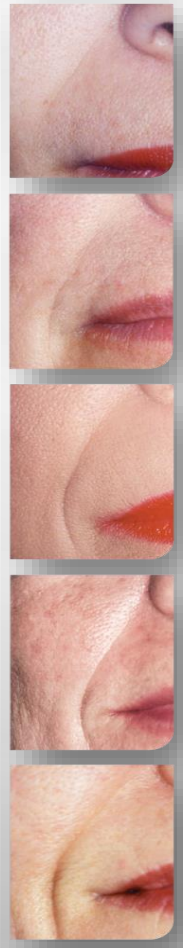
Grade 1 ~ 0.3 cc per side

Grade 2 ~ 0.6 cc per side

Grade 3 ~ 0.6 cc per side

Grade 4 ~ 1.0 cc per side

Grade 5 ~ 1.0 cc per side



How severe is the crease

How much filler is needed

What result to expect

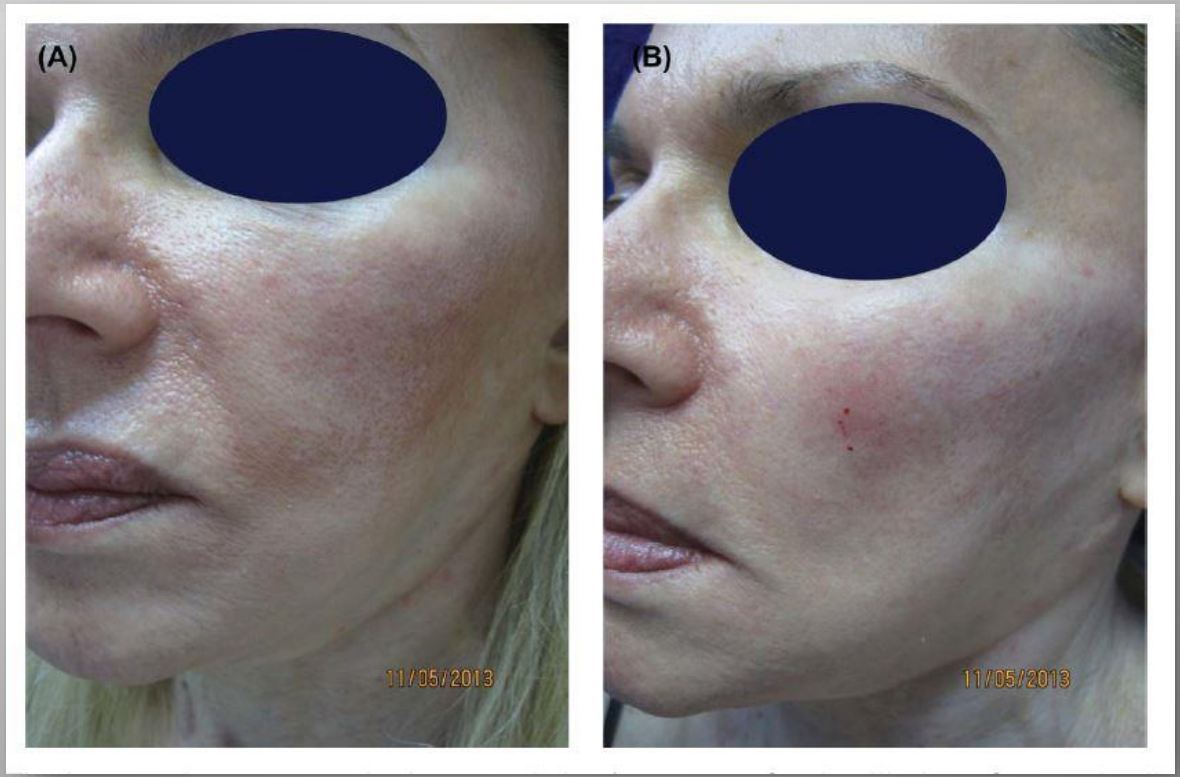
Tricks to Demonstrate Effect

Use of Xylocaine to Predict the Effect of Neuromodulators

Wirtzer, 2015

Tricks to Demonstrate Effect

Use of Saline to Predict the Outcome of Filler Injections



Wirtzer, 2015

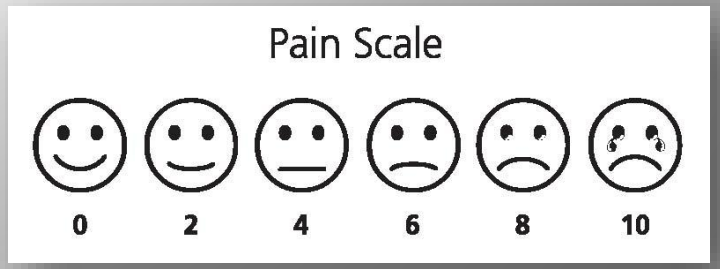
Patient Comfort

Minimize discomfort, redness, swelling, bruising

- Filler viscosity
  - Thicker HAs (Restylane) & CaHA (Radiesse) more pain
- Needle caliber
  - CaHA needs at least 27G needle
  - PLLA at least a 25G to 27G needle
- Anatomical site
  - Perioral, periocular & lip more painful than NLF
- Pre & postinjection cooling packs for 5 to 10 min

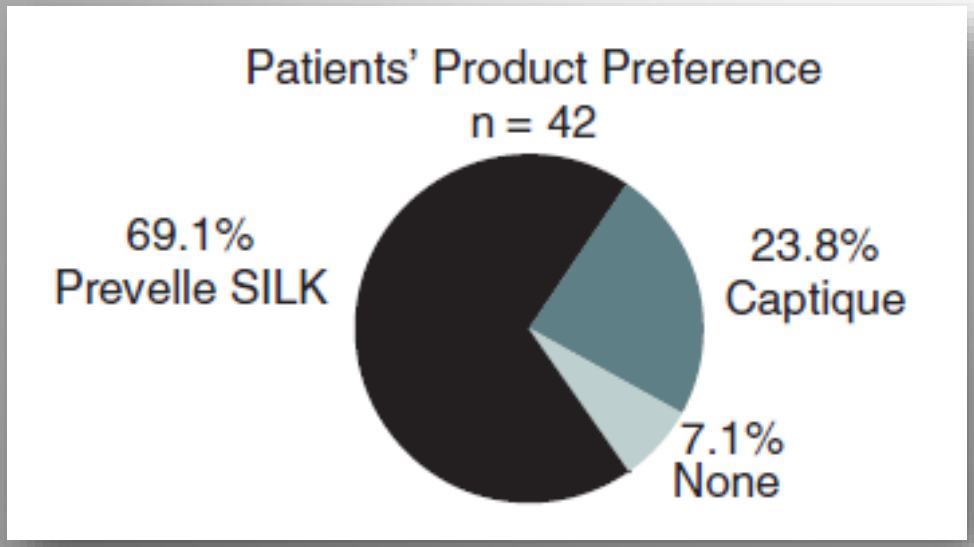
Patient Comfort

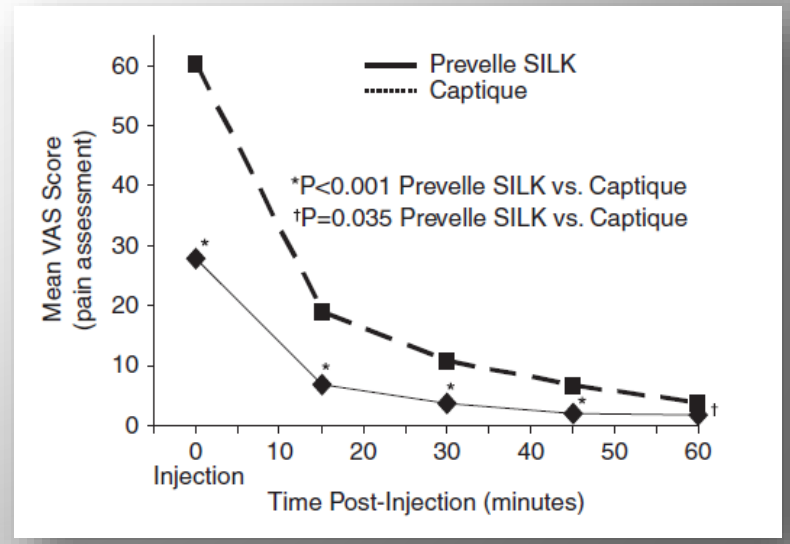
- No anesthetic
- Topical cooling
- Topical anesthetic
  - Applied 30 – 60 min before injection
  - Occlusive dressings (Tegaderm)
  - Injection pain may be experienced deeper than level of effect
- Injection site block
  - 0.3 cc 1% lidocaine + epi with 32G needle
- Nerve blocks
  - Infraorbital nerve: NLF & upper lip
  - Mental nerve: lower lip & marionette lines
  - May cause tissue distortion



Hyaluronic Acids + Lidocaine

- Patient-blinded, prospective, randomized, split-face design
- HA + lidocaine (Prevelle SILK) vs no lidocaine (Captique)
- 50% less pain with lidocaine than with without
- No difference in NLF outcome after 2 weeks

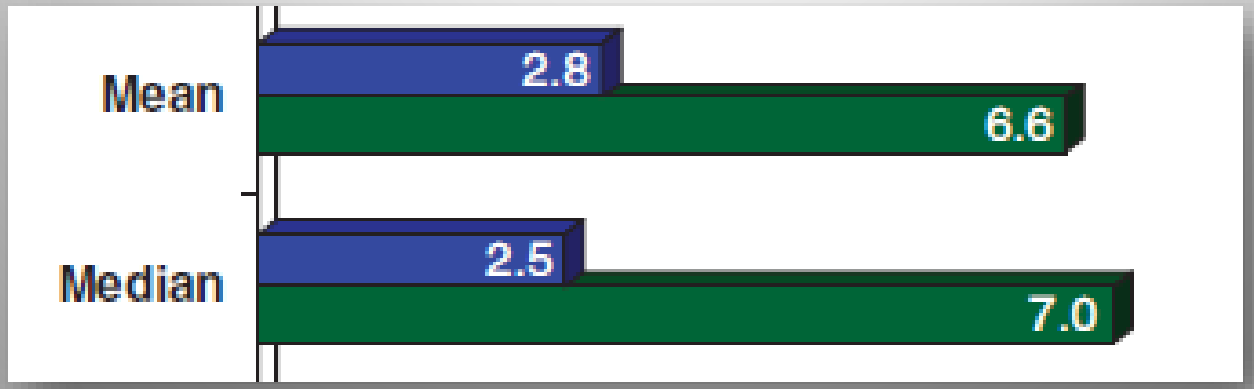




Monheit 2010

Calcium Hydroxylapatite + Lidocaine

- Calcium hydroxylapatite (CaHA, Radiesse)
- Prospective, randomized, split-face, single-blinded
- CaHA vs CaHA + 0.2 cc 2% lidocaine for NLF
  - Can premix day in advance
- 4 point reduction in pain at time of injection

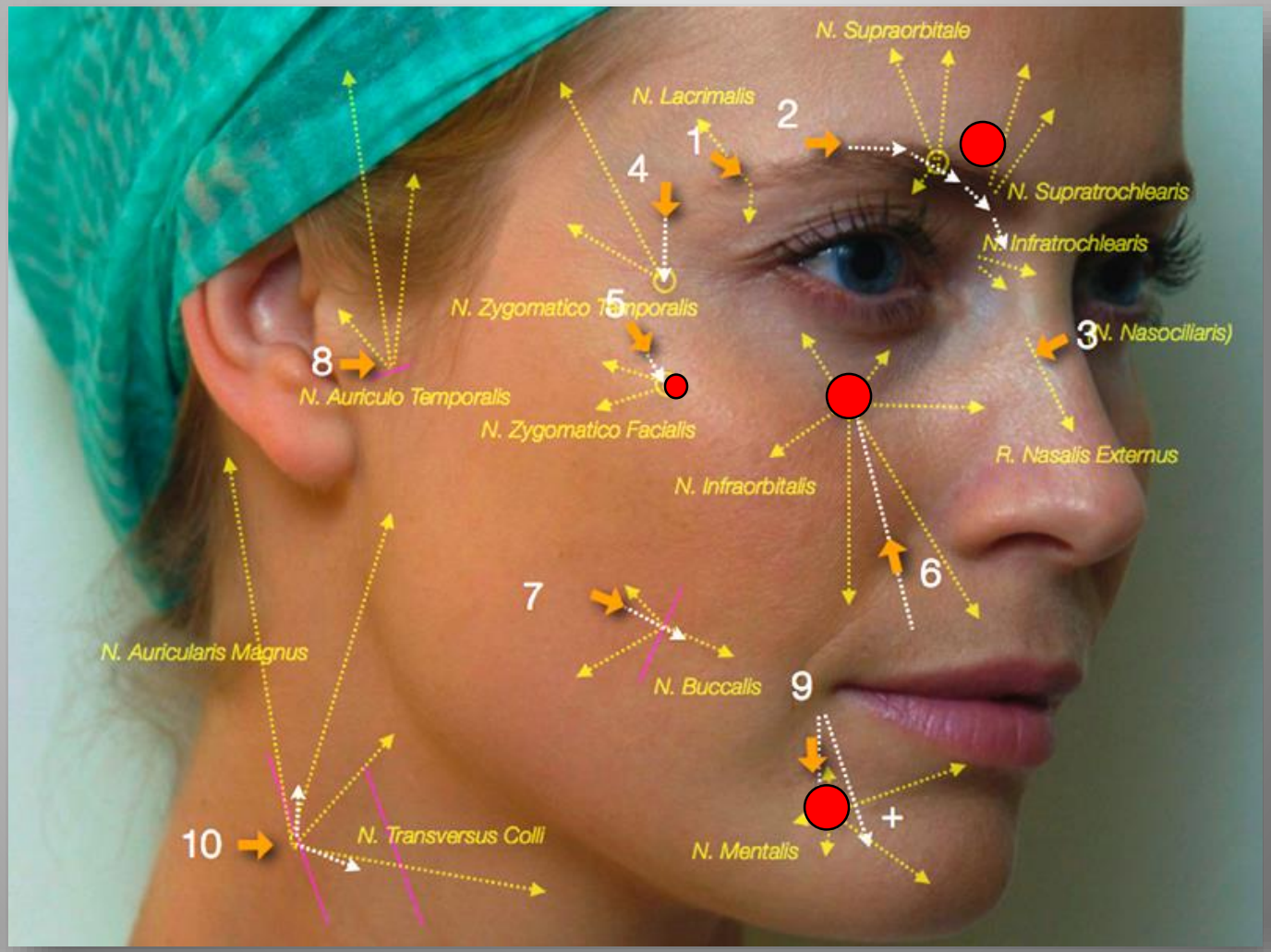


Marmur 2010

Basic Set Up


+ Gloves
McKESSON
Alcohol Prep Pad
1.8" x 3.5"
MFR # 58-404
Povidone-Iodine Swabstick
Antiseptic/Germicide For External Use Only
McKESSON
Medi-Pak
Instant Cold Compress
Single Use • Disposable
Latex-Free
For temporary relief of minor pain and swelling caused by:
• Minor Burns • Strains • Toothaches • Contusion • Insect Bite
4" x 6" (10.2 cm x 15.2 cm)
Reorder No. 16-9701
FOR EXTERNAL USE ONLY.
Marketed By
McKesson Corporation
PARTELL
SPECIALTY PHARMACY
SAMSON CHAN, MD*
For office administration (Not For Resale)
No refills authorized
Fruit of the Earth
ALOE VERA
100% GEL
PURE. No Color Added.
Moisturizing Therapy for Sunburn • Dry • Irritated Skin
24 OZ. (680g)

Block & Tackle the Face

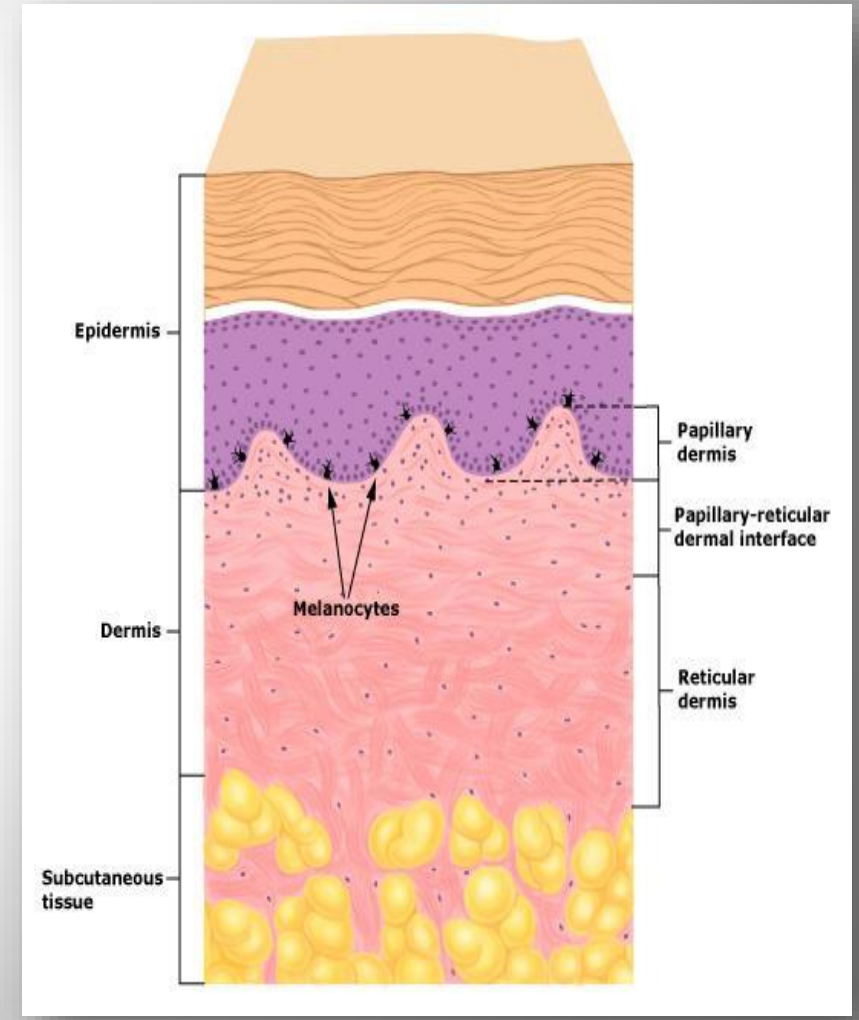


Jesper Sorensen
Zide 1998

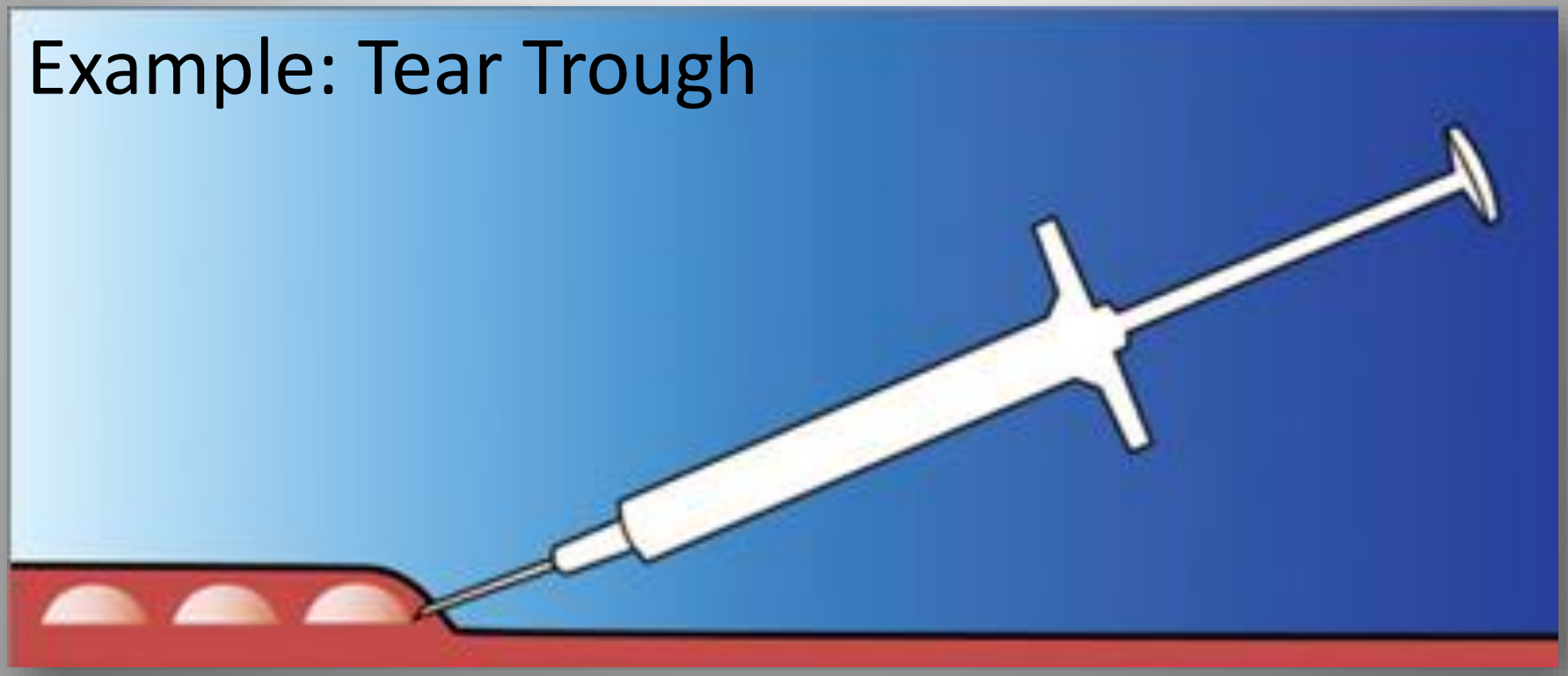
Injection Technique

Target the correct level

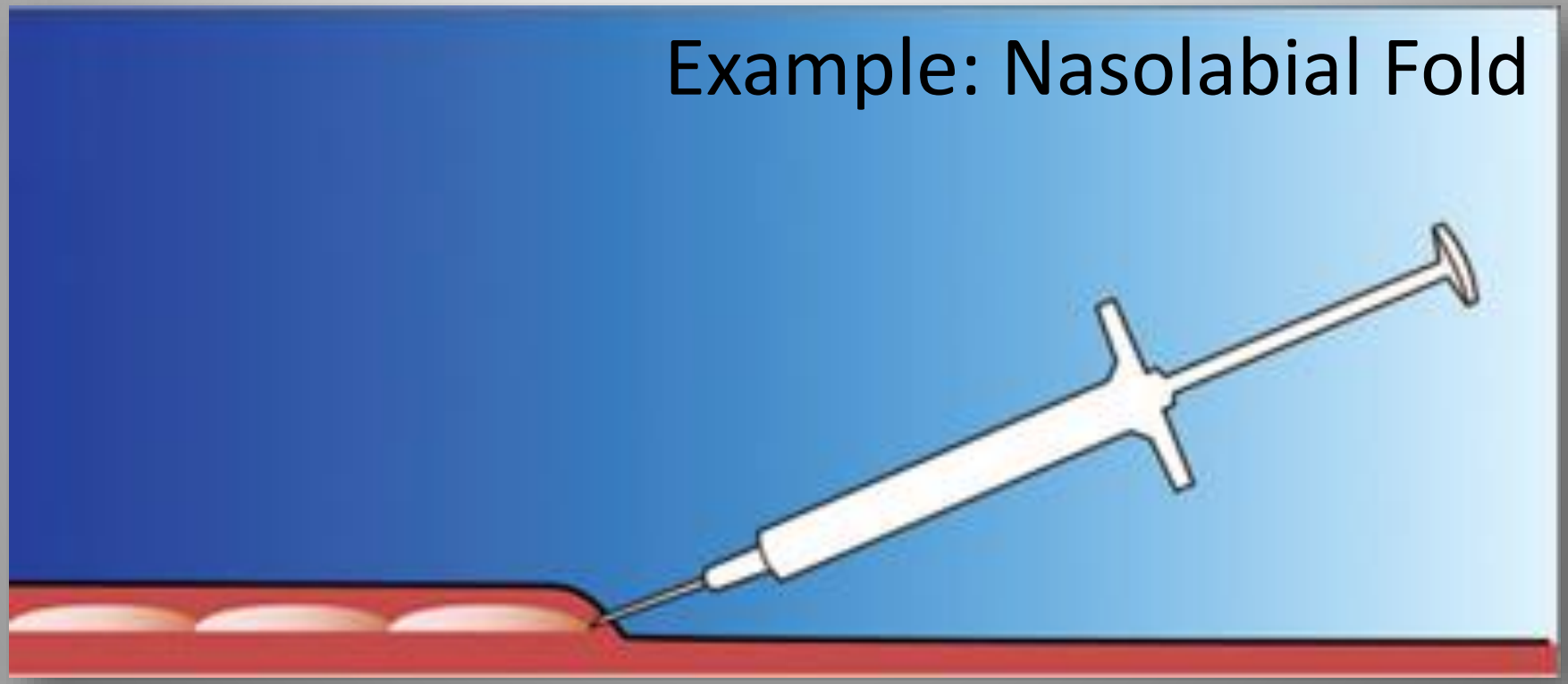
- Mid to deep dermis
  - Low G' HAs
- Subcutaneous
  - PLLA, CaHA, PMMA
  - Higher G' HAs
- Deep/preperiosteal
  - High G' HAs, CaHA



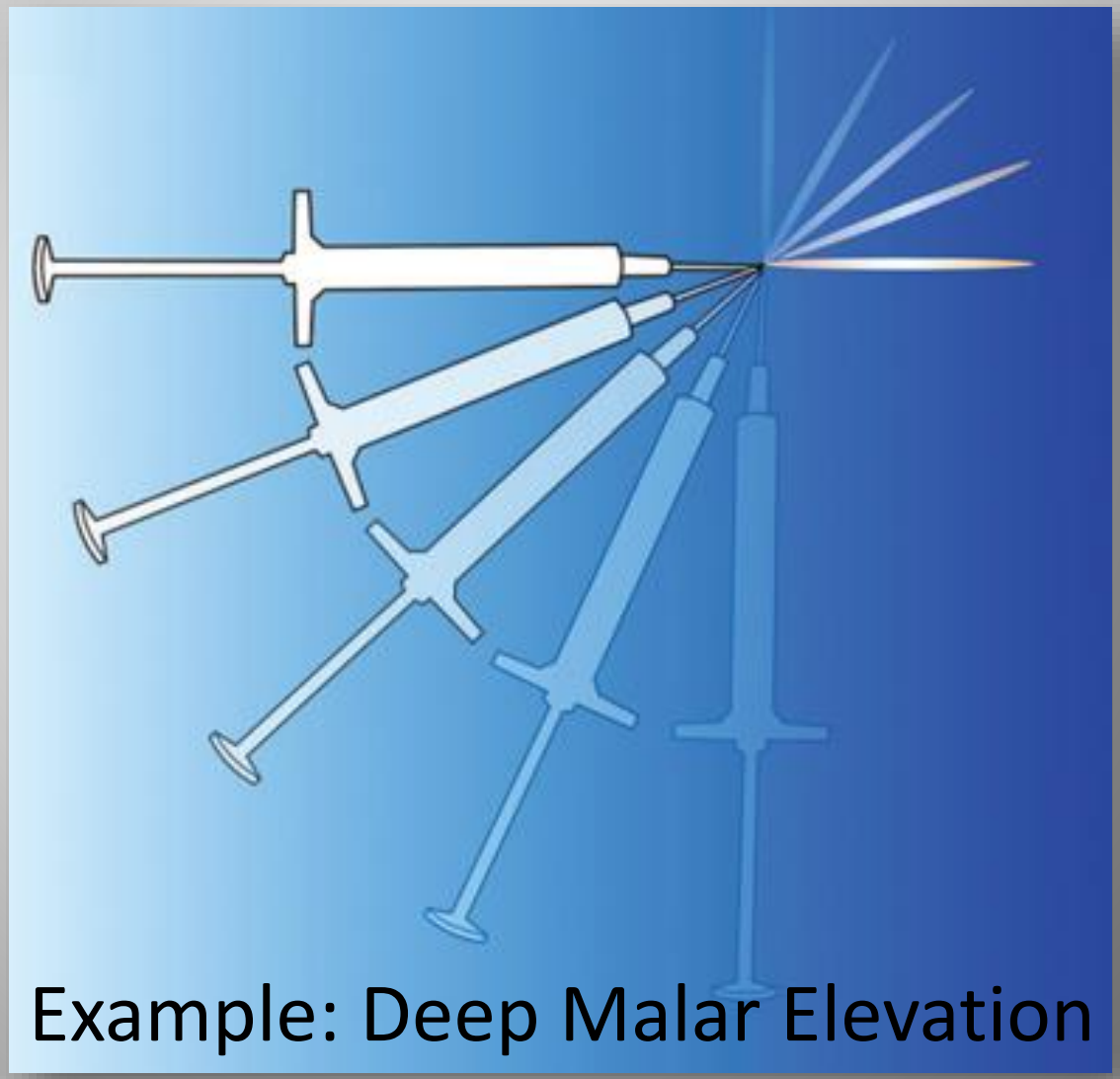
Serial Puncture



Linear Threading

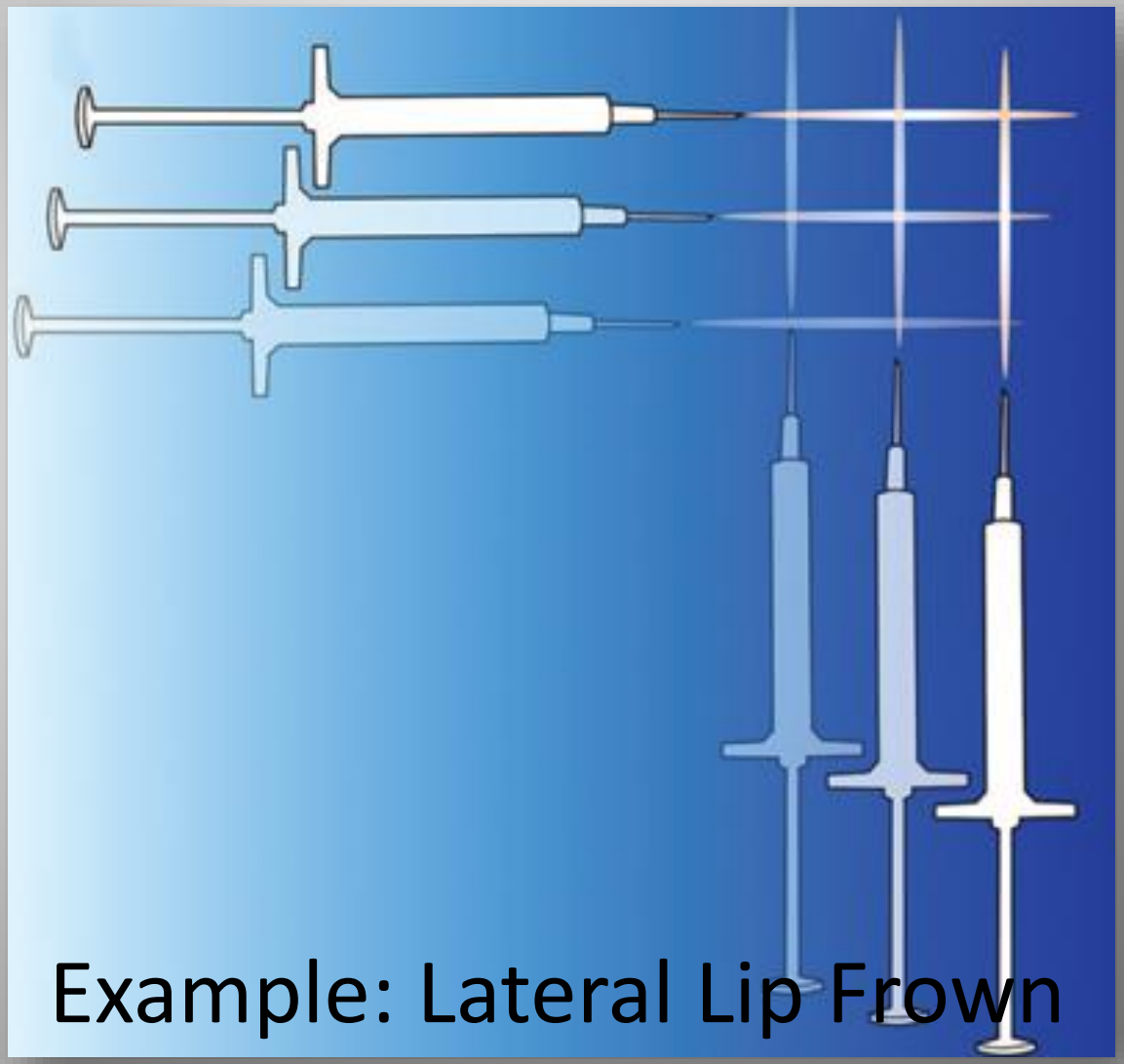


Fanning

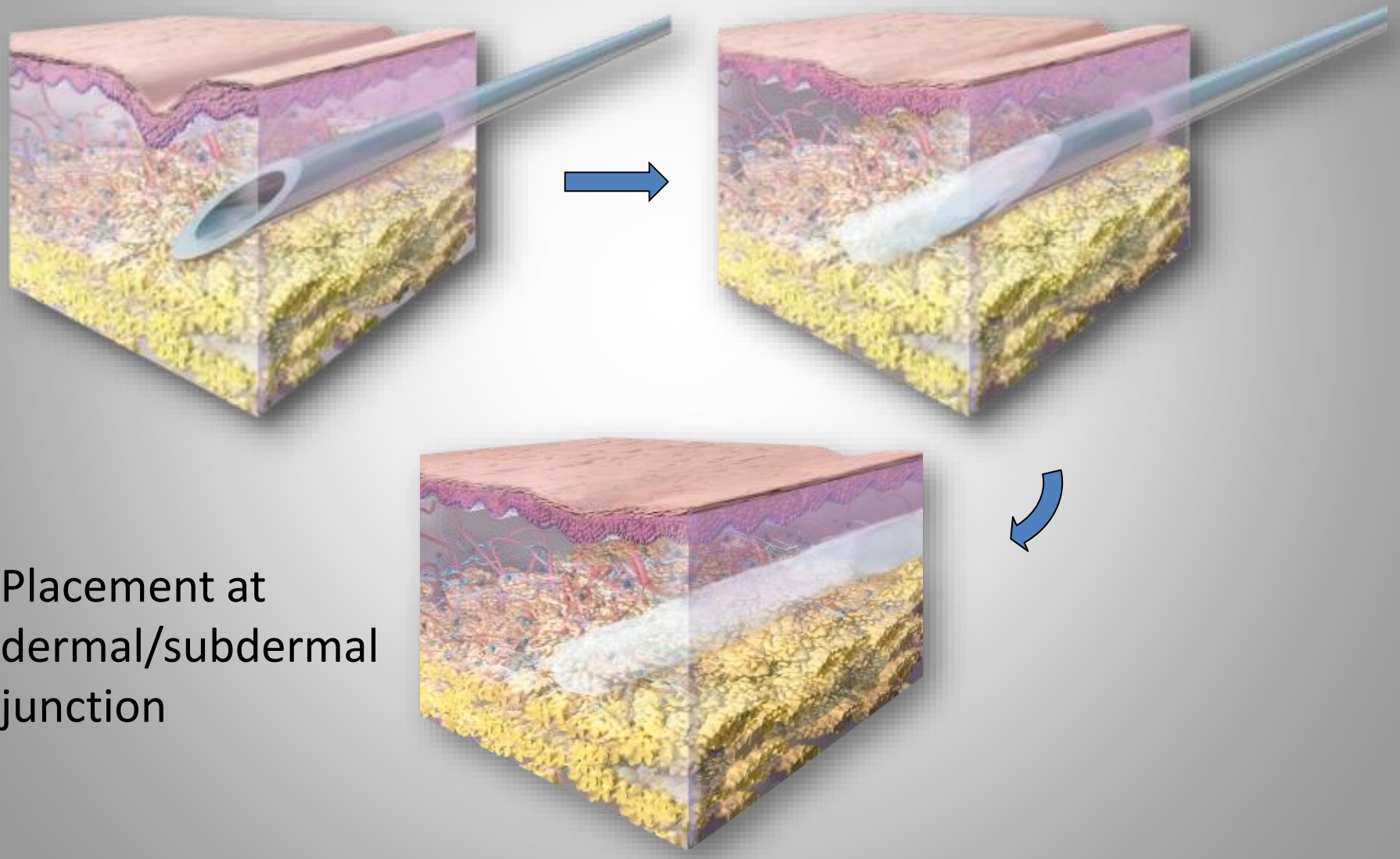


Example: Deep Malar Elevation

Cross Hatching



Tunneling or Linear Threading



Placement at dermal/subdermal junction

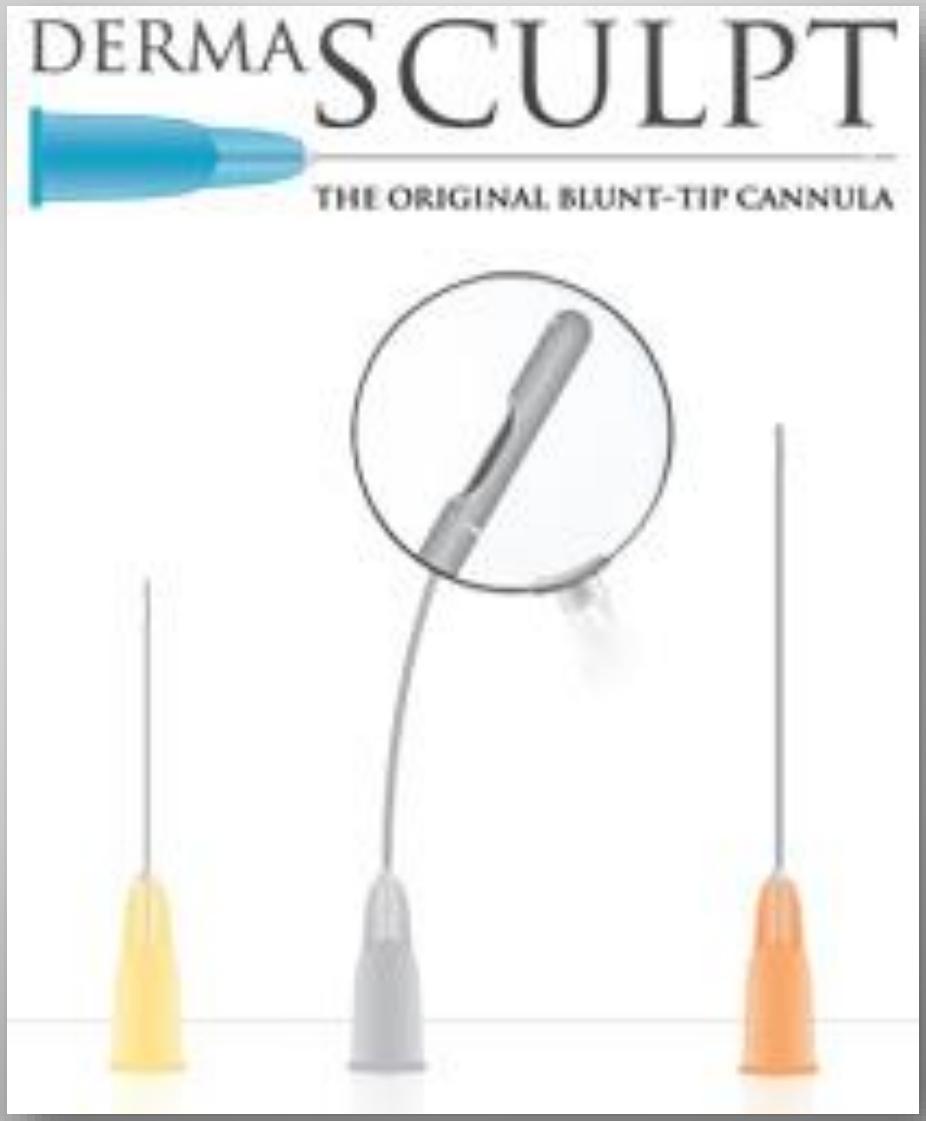
Proper Dermal Injection

Too Superficial

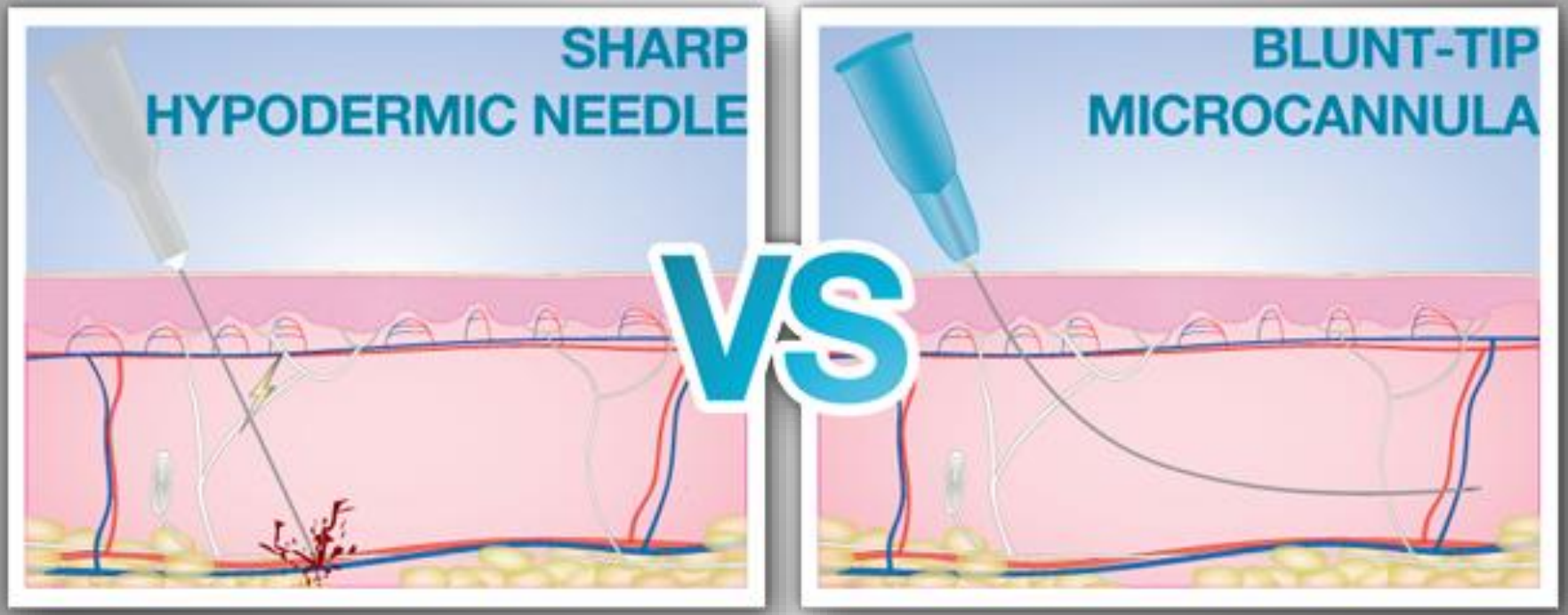
Too Deep

Correct Placement

Blunt Injection Cannulas



Blunt Injection Cannulas



Blunt Injection Cannulas

Safety and effectiveness of injection of calcium hydroxylapatite via blunt cannula compared to injection by needle for correction of nasolabial folds

Kenneth R Beer, MD

Esthetic, General & Surgical Dermatology, West Palm Beach, FL, USA

- 20 patients – split face (not enough for adverse events)
- Needle side had more pain, redness, swelling
- Cannula side had better correction at 19 days

Results

Filler or Fat?

Hollow Temples

Lower Lids & Tear Troughs

Proceed with Caution

Tear Trough & Lower Lids

- Inject on periosteum
- Expect edema & ecchymosis
- Under correct
  - Touch up in 2 weeks
- Prolonged edema
  - Treat early
  - Hyaluronidase
- May persist for years

Not for novice injectors

Malar & Cheek

Best Bang for the Buck

Malar Injections Improve Nasolabial Folds

A randomized comparison of the efficacy of low volume deep placement cheek injection *vs.* mid- to deep dermal nasolabial fold injection technique for the correction of nasolabial folds

Molly Goodier, BS,[1] Kendra Elm, BS,[1] Irmina Wallander, BA,[1] Brian Zelickson, MD,[1,2] & Sarah Schram, MD[1,2]

- Does NLF need direct injection?
- Can cheek injection improve NLF?
- Split face HA (Juvederm Ultra Plus)
- Similar improvements at low volume injections
  - Average 0.6 cc per injection site

Injection Areas

NLF injection

Mid-lateral cheek injection

Improved Nasolabial Folds

Before & After: R NLF injection, L cheek injections

Improved Nasolabial Folds

Before & After: R NLF & cheek injection, L cheek injections

Malar & Cheeks

- Malar
  - High G' (Radiesse or Lyft, Bellafill for long-term)
  - 0.1 cc needle bolus at 2-4 points on periosteum at malar prominence
  - Massage & shape to desired form
- Cheeks
  - Moderate to high G' blunt cannula injection
  - Subcutaneous fanning or cross-hatching
- Treat before nasolabial folds

Nasolabial Folds

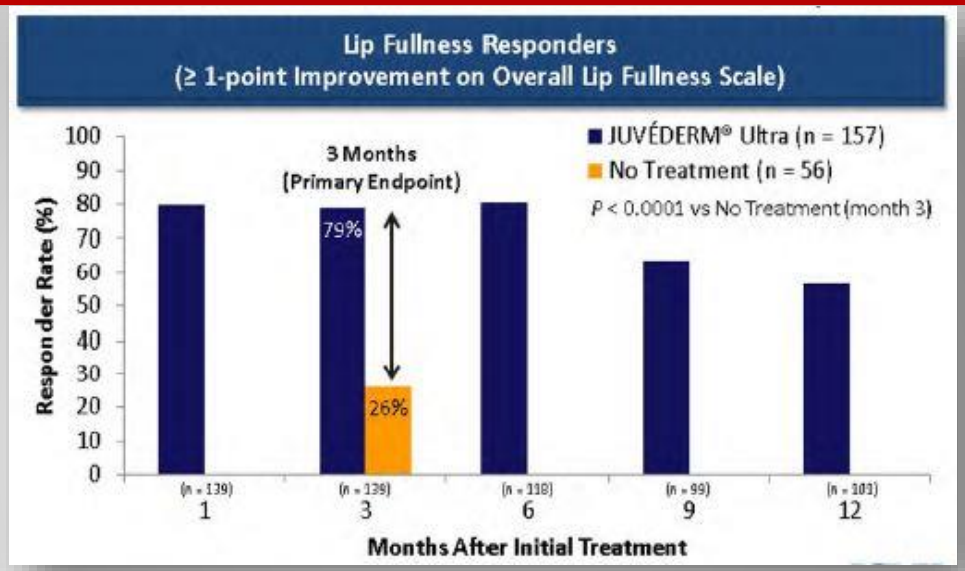
After Malar Correction

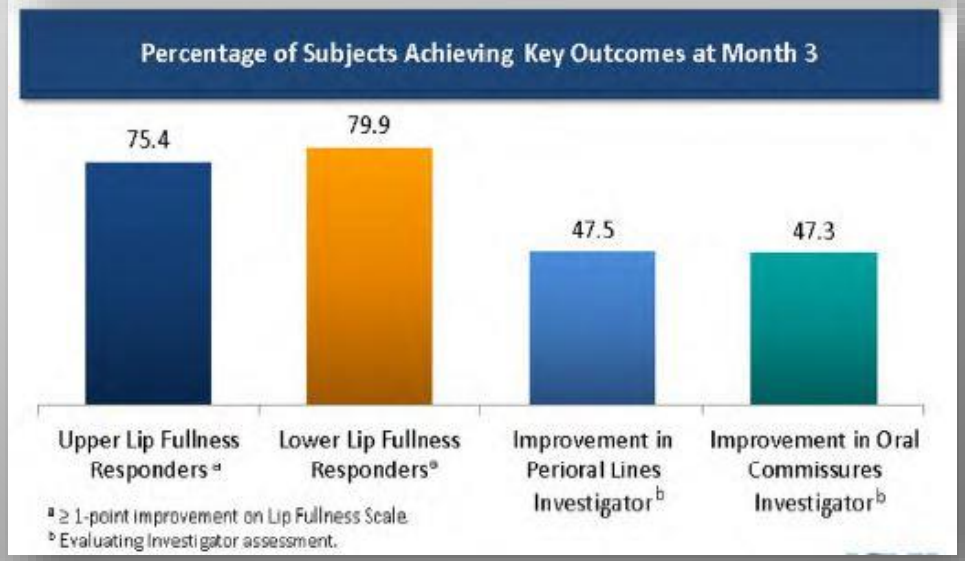
Lips & Perioral

Juvederm Ultra XC for Lips

- Previous indication
  - Mid to deep dermis, facial wrinkles & folds
- Has lidocaine
- Single blinded MC-RCT
  - 157 Juvederm patients + 56 controls (then crossed over)
  - Touch up at 2-4 weeks if needed
  - Validated 5 point scale
  - **Total volume (initial + touch up): 2.1 cc**
    - Upper lip 0.9 cc Lower lip 0.7 cc
    - Upper lip lines 0.2 cc Lower lip lines 0.1 cc
    - Oral commissure 0.4 cc

Juvederm Ultra XC for Lips





Lasts up to 1 year

Lip Improvement

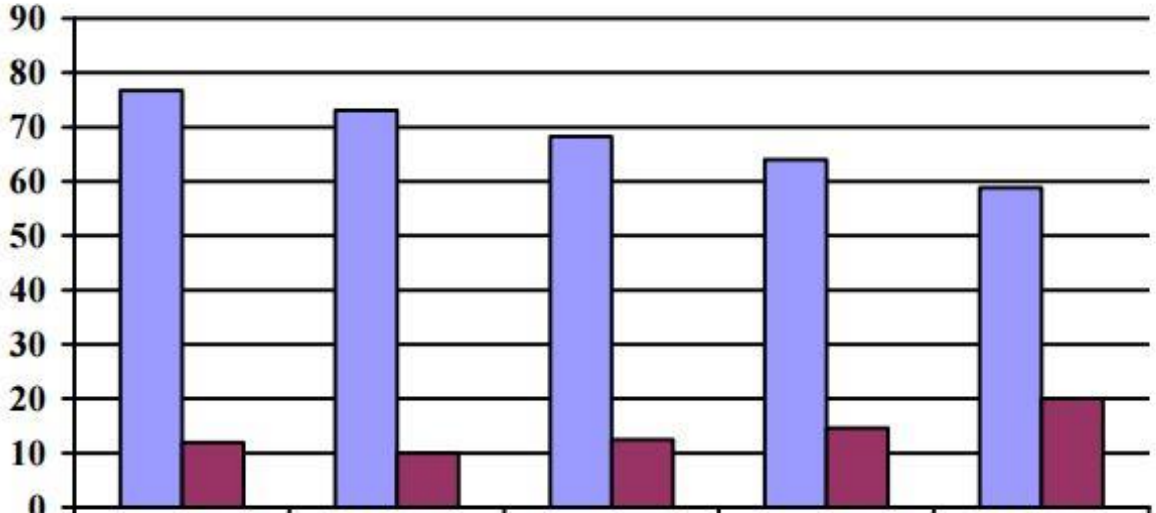
- 3 Months - 79%
- 1 year - 78%

Restylane Silk Approval

- RCT 221 subjects at 14 centers
- Effectiveness: ≥1 grade improvement
- Injection volume
  - Upper & lower lip: Mean 2.2 cc
  - Perioral lines: Mean 0.5 cc

Restylane Silk Approval: Lips

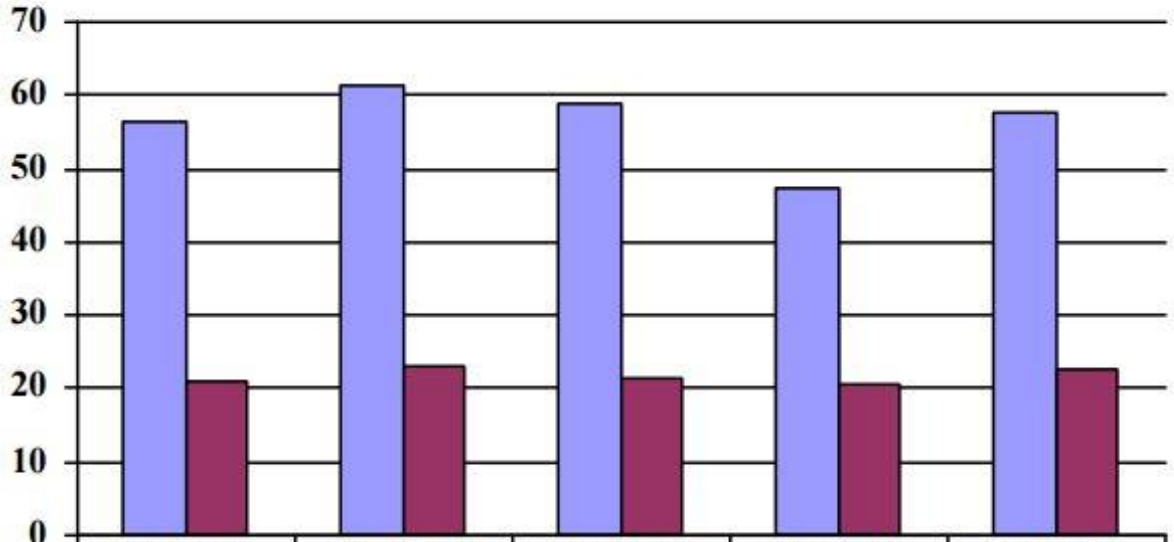
Proportion (%) of MLFS Responders Measured by the Blinded Evaluator (Upper and Lower Lip Combined)



	Week 8	Week 12	Week 16	Week 20	Week 24
Restylane Silk Treatment	76.7	73.1	68.3	64	58.8
No Treatment	11.9	10	12.5	14.6	20

Restylane Silk Approval: Perioral Lines

Proportion (%) of Responders Measured by the Blinded Evaluator for Upper Perioral Rhytids



	Week 8	Week 12	Week 16	Week 20	Week 24
Treatment of Rhytids + Lip	56.5	61.3	59	47.5	57.6
Treatment of Lip Only	20.9	22.9	21.4	20.6	22.8

Jaw Line & Pre Jowl Sulcus

Small Volume, Big Result

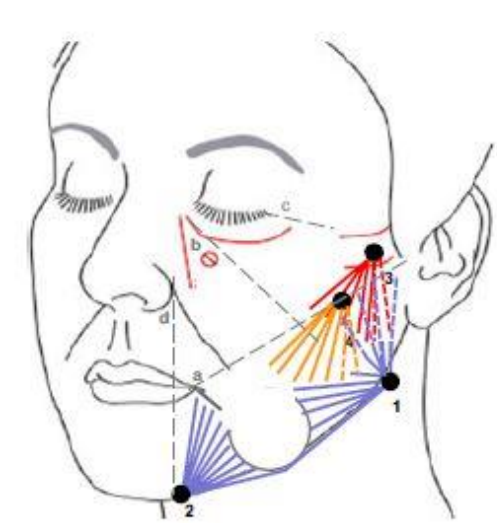
Jawline Enhancement

Calcium hydroxylapatite for jawline rejuvenation: consensus recommendations

Jean-Marie Dallara, MD,[1] Martine Baspeyras, MD,[2] Patrick Bui, MD,[3] Hugues Cartier, MD,[4] Marie-Hélène Charavel, MD,[5] & Laurent Dumas, MD[6]

- Diminish effects of jowls on jawline
- Caution with “full” and “square” faces
- Consider saline injection test

Jawline Enhancement



Point 1: Mandibular angle

Point 2: Prejowl sulcus

Point 3 +/- 4: Posterior cheek vector

If necessary after further evaluation:

Point 5: Cheek bone
Point 6: Mid-cheek groove

Line a: Labial commissure –Tragus
Line b: Mid-cheek groove
Line c: External cantus – border of the superior zygomatic arch 2.5 cm)
Line d: Vertical line descending from the outer edge of the nostril

Before & After 4.5 cc (total)
3 Syringes for face

Nose

Proceed with Caution

Hands

Why Stop at the Face?

Aging Hands

Treating Age Spots

Hand Rejuvenation

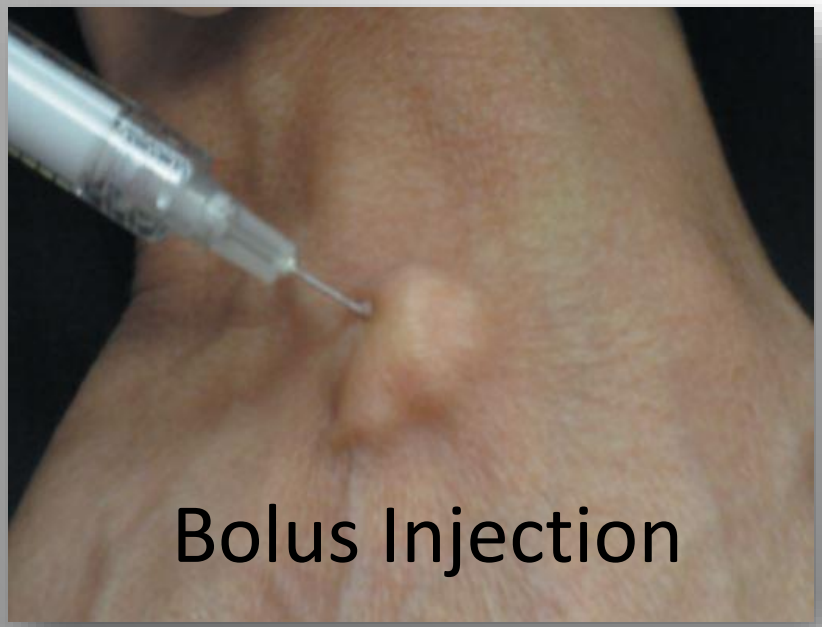
After 3 SculptraVials

Hand Augmentation

Hand recontouring with calcium hydroxylapatite (Radiesse)®

Kenneth L Edelson, MD, FAACS

Private practice, New York City



FDA panel approval for Radiesse 2015

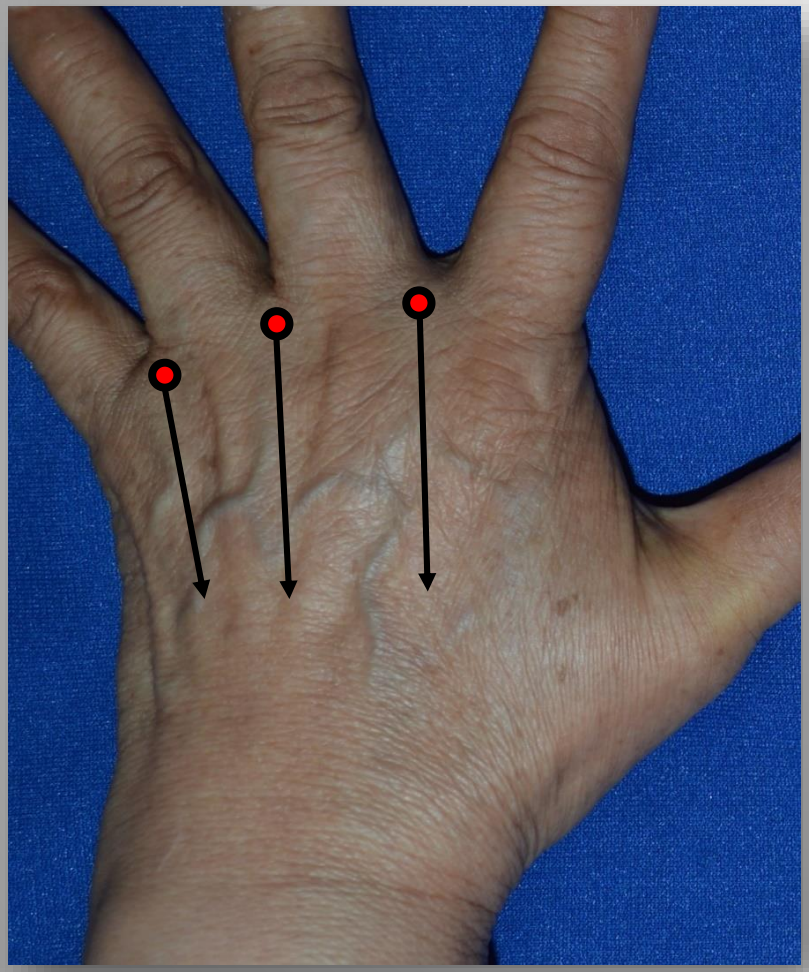
Radiesse for Hands

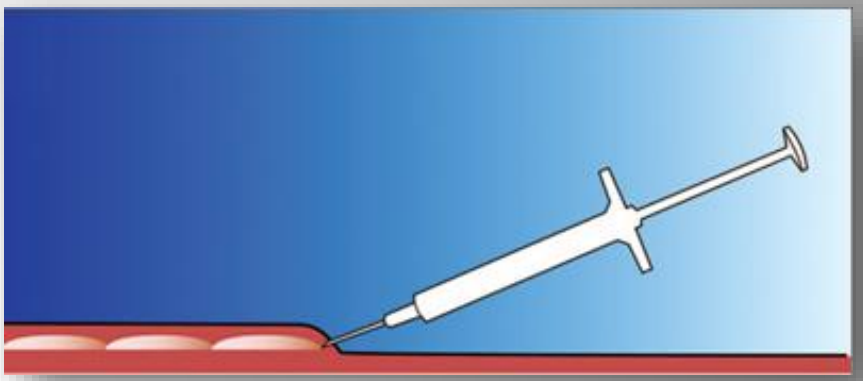
RCT at 6 sites

- 85 patients, maximum 3 cc Radiesse per hand
- Mean age: 53-54 years
  - Mostly white females
- 3 months
  - 75% had ≥1 point improvement (vs 3.4% of controls)
  - 76% rated “much” or “very much improved”
- Lasts up to 1 year
  - Some had retreatment
- Has lidocaine

Aging Hand

Aging Hand





High G’
Blunt cannula
Linear threading
Massage to position

Restore Dorsal Hand Fullness

Before and after 1.5 cc **Radiesse** to dorsum (FDA Approved)

Restore Dorsal Hand Fullness

Before and after 1.5 cc **Radiesse** to dorsum (FDA Approved)

Fat Graft Dorsal Volumization

Before and 6 months after **Fat Grafting** to dorsum

Fat Graft Dorsal Volumization

Before and 6 months after **Fat Grafting** to dorsum

Ultherapy Over Filler

Microfocused Ultrasound With Visualization and Fillers for Increased Neocollagenesis: Clinical and Histological Evaluation

Gabriela Casabona, MD,* and Niceo Michalany, PhD†

Can MFUS interact with subcutaneous filler?

- Single patient with Voluma & Radiesse
- No negative effect seen on histology
- Enhanced collagen & elastin

Realistic Expectations!

Complications

The Itinerant Patient

- Patient with unknown filler administered elsewhere (or abroad) requests ‘‘touch-up’’
  - Additional HA can introduce bacteria & activate biofilm
  - Original filler material may be unknown (unapproved)
  - May have had more than 1 product used
- Results in complex evaluation & treatment plan
  - Patient perception: “It was just some injections…”

Filler Complication Categories

Immediate Onset (0 – 2 Days)

Early Onset (3 – 14 Days)

Delayed Onset (> 14 Days)

Immediate Complications

- Over or Under Correction
- Implant Visibility
  - Injection too superficial
    - **HA** blue discoloration
      - Massage, Hyaluronidase
    - Particulate fillers (**CaHA, PMM**) white bumps
      - Needle unroofing & evacuation
- Vascular Compromise
  - Glabella most common?

Glabellar Vascular Compromise

Glabellar Vascular Compromise

Glabellar Vascular Compromise

Vascular Compromise

	Arterial Occlusion	*Venous Occlusion*
Presentation	Immediate or early, blanching, severe pain	Delayed, dull pain, dark discoloration
Management	Stop injection, attempt aspiration	Massage
	Massage	Warm compresses
	Warm compresses	2% nitroglycerin paste*
	2% nitroglycerin paste*	Injection of hyaluronidase (if caused by hyaluronic acid product)
	Injection of hyaluronidase (if caused by HA product)	Consider hyperbaric oxygen in cases of impending massive skin necrosis
	Antibiotic therapy (topical, parenteral, or both) in cases of skin breakdown	Antibiotic therapy (topical, parenteral, or both) in cases of skin breakdown
	Conservative debridement	Conservative debridement
	Frequent follow-up	Frequent follow-up
Prevention		
	Informed consent	Informed consent
	Smallest possible needle	Smallest possible needle
	Smallest possible volume injected	Smallest possible volume injected
	Proper plane of injection	Proper plane of injection

Sclafani 2009

Early Onset Complications

- Temporary nodules
- Persistent nodules
  - Non inflammatory
  - Inflammatory
    - Fluctuant vs nonfluctuant
    - Treat as infection
- Angioedema

Delayed Onset Complications

- Persistent nodules
  - Non inflammatory
  - Inflammatory
    - Fluctuant vs nonfluctuant
    - Treat as infection
- May develop into chronic problem
  - Abscess, tissue loss
- Persistent malar swelling

Case Example 1

42 year old female

- HA (Restylane) injection for acne scars
- 3 hours later - white patch over injection site
- What do you do?

Case Example 1

42 year old female

- HA (Restylane) injection for acne scars
- 3 hours later - white patch over injection site
- What do you do?
  - Nitropaste
  - Warm compressed
  - Hyaluronidase

Immediate blanching upon injection or delayed reticulated duskiness after injection can identify impending necrosis

Case Example 1

42 year old female

- HA (Restylane) injection for acne scars
- 3 hours later - white patch over injection site
- 4 days later - skin slough
- Now what?

Case Example 1

42 year old female

- HA (Restylane) injection for acne scars
- 3 hours later - white patch over injection site
- 4 days later - skin slough
- Conservative skin care

  \+ Hydroquinone

Case Example 2

46 year old female

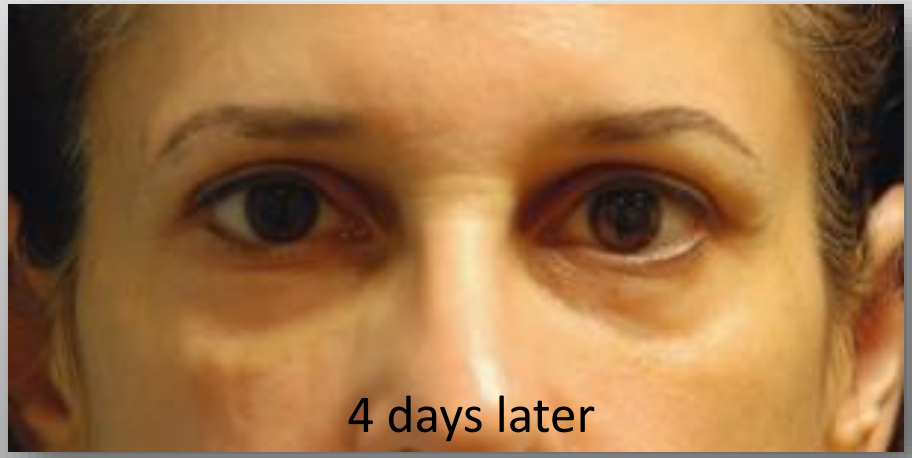
- Multiple HA* injections to lower eyelids over 3 years
- 1 month later developed periorbital swelling
- Allergy testing negative
- What now?

* Restylane & Juvederm

Case Example 2

46 year old female

- Multiple HA* injections to lower eyelids over 3 years
- 1 month later developed periorbital swelling
- Allergy testing negative
- What now? **15 units Hyaluronidase per lower lid**



4 days later

* Restylane & Juvederm

Persistent HA

Restylane persisting in lower eyelids for 5 years

Steven H Dayan, MD, FACS,[1,2,3,4] John P Arkins, BS,[4] & Michael Somenek, MD[2]

After 5 years, fullness resolved 2 weeks after 60U hyaluronidase injected per side

HA Migration

Delayed Migration of Hyaluronic Acid Fillers: A New Complication?

- 3 patients with tear trough injections resulting in inferior migration years later
- Resolved with hyaluronidase

Case Example 2

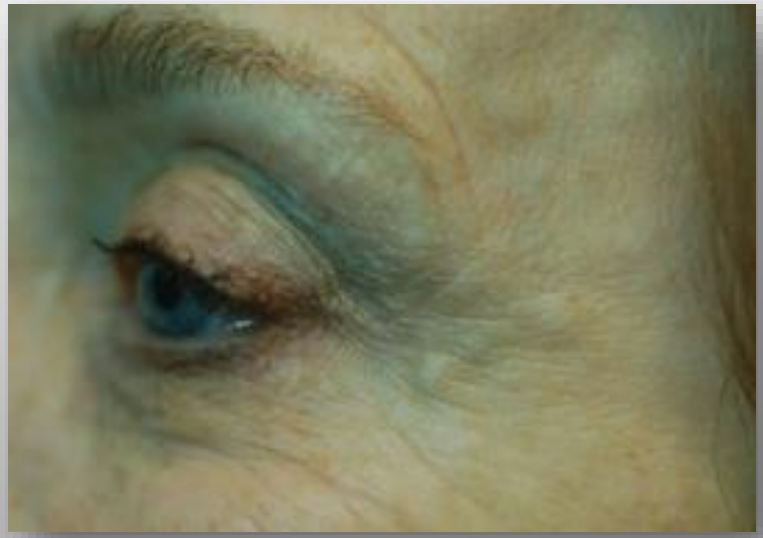
Lessons Learned from Infraorbital Filler Injections

- Volume replacement is challenging
- Higher potential for complications
- Eyelid skin is unforgiving (produces lumps & bumps)
- Superficial injections produce persistent fullness
- Careful injection technique (small amounts deep)
- Variable longevity in this location
- **Unpredictable edema**

Case Example 3

67 year old female

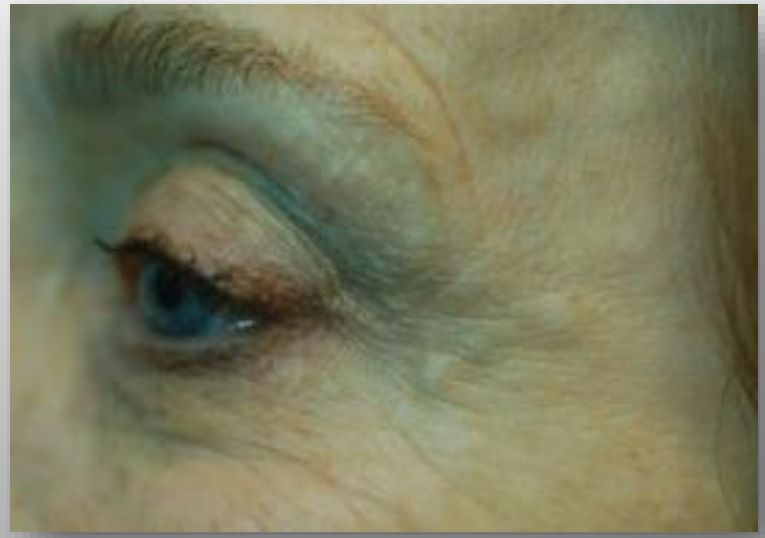
- 1 vial (in 5cc) PLLA (Sculptra) injected
- Palpable nodules 10 months later
- What now?



Case Example 3

67 year old female

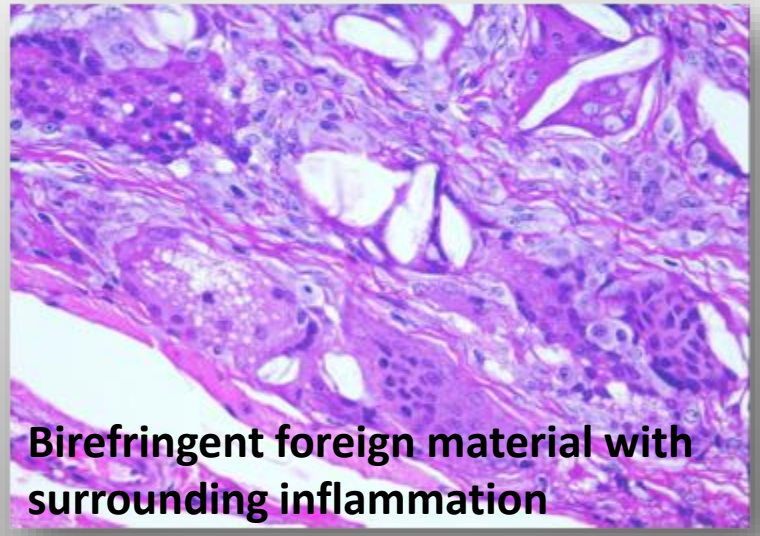
- 1 vial (in 5cc) PLLA (Sculptra) injected
- Palpable nodules 10 months later
- Steroid injection ⟹ No Effect



Case Example 3

67 year old female

- 1 vial (in 5cc) PLLA (Sculptra) injected
- Palpable nodules 10 months later
- Steroid injection → No Effect → Excision



Birefringent foreign material with surrounding inflammation

Case Example 3

Lessons Learned from PLLA Injections

- Use higher dilution (8-10cc per vial)
- Dilute 3-5 days in advance
- Inject in deep plane
- Subperiosteal periorbital injection
- Frequent massage

Sculptra®
injectable poly-L-lactic acid

Sculptra Nodules

- Inject saline
- 5-FU
- Kenalog

Case Example 4

64 year old female

- Multiple HA injections in NLF
- What is this?

Case Example 4

64 year old female

- Multiple HA injections in NLF
- What is this? **Tyndall Effect** (Blue discoloration)

Case Example 4

64 year old female

- Multiple HA injections in NLF
- How to treat?

Case Example 4

64 year old female

- Multiple HA injections in NLF
- How to treat? **15 units Hyaluronidase**

Case Example 4

Lessons Learned from HA Injections

- Superficial injections can be visible
- Small volume injections, evaluate & re-inject if needed
- Hyaluronidase
  - 10 to 30 units (4 to 7 days to effect)
  - Local skin reactions common
    - **Amphadase** (bovine - skin test)
    - **Hylenex** (r-human)
    - **Vitrase** (ovine - skin test)

Case Example 5

51 year old female

- Pain, redness & swelling 2 weeks after HA injection
- Firm without fluctuance
- Treatment?

Case Example 5

51 year old female

- Pain, redness & swelling 2 weeks after HA injection
- Firm without fluctuance
- Cellulitis, no abscess
  - Antibiotics x 6 weeks
  - Minocycline + clarithromycin

Case Example 5

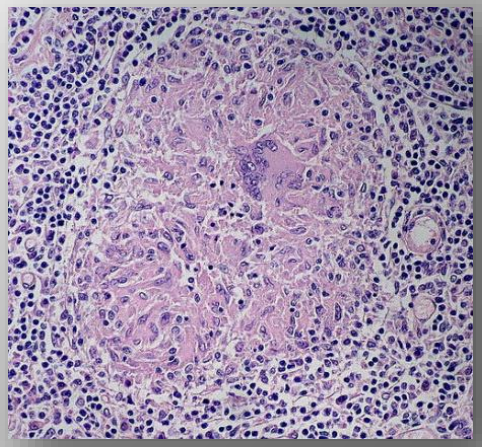
Lessons Learned from Infections after HA Injections

- Sterile skin prep before injection
  - Remove make up
- Culture fluctuant nodules before antibiotics
- Steroids not useful, prolong infection
- Consider atypical mycobacteria & biofilm if infection occurs weeks after injection
  - Multiple antibiotic therapies
  - Enzymatic removal of biofilms controversial
    - Bioflim dissolution → macrophage migration & antibiotic penetration

      verus
    - Bacterial spread

Granulomas vs Infections

- Resorbable fillers
  - Low incidence of long-lasting or late complications
- Partially or completely nonresorbable fillers
  - More anaerobic infections & granuloma reactions
  - Harder to treat
- Bacterial infection tissue swelling
  - Edema & cellular foreign-body response
- Micro particle filler swelling
  - Foreign body granuloma



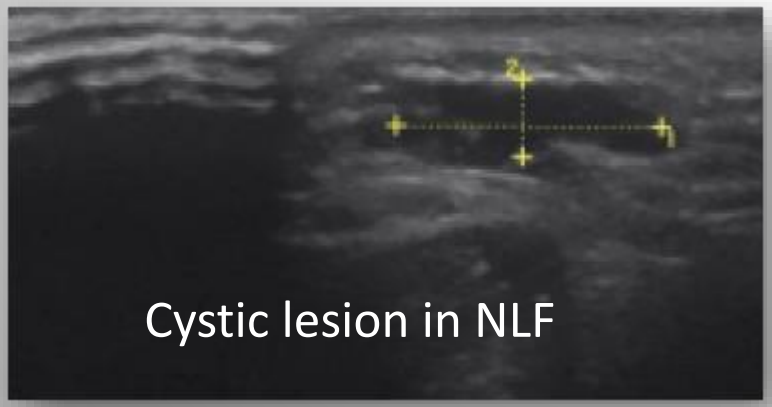
Granuloma

Granulomas vs Infections

- Infection
  - Progress slowly
  - Anaerobic growth conditions
  - Symptoms 1 to 2 weeks after injection
- Granuloma
  - No detectable bacteria
  - May appear years after injection
  - Associated with microparticles fillers

Long Lasting Low Grade Infections

- Culture negative nodules
- Mistaken for foreign-body granulomas
- Bacteria in biofilm
- Cysts on US



Cystic lesion in NLF

Bacteria in Biofilm

Noninvasive therapeutic options

- Aspiration
  - Rarely works after a few months
- Excision
  - Scars & disfigurement
- Antibiotics
  - Effective only before biofilm develops
- Steroids
  - Temporary effect, rebound, skin atrophy & telangiectasias
- 5-Fluorouracil
  - Temporary effect & rebound

New Concepts on Filler Problems

Many problems assumed to be foreign body granulomas or allergic reactions on the basis of negative bacterial cultures are now thought to be due to biofilms

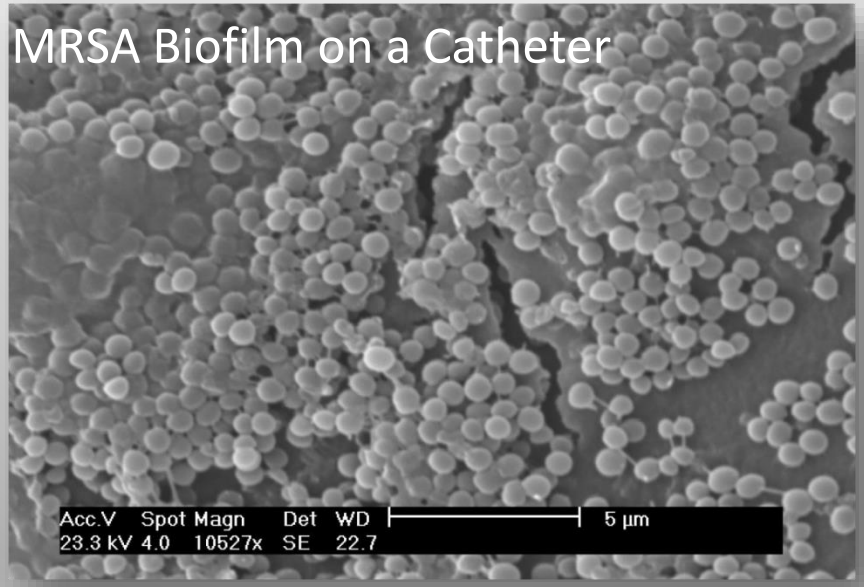
(Wiest, 2009)

Biofilms are almost impossible to culture using current standard culture technology and may be treated incorrectly with steroids injections, instead of 2 or 3 antibiotics

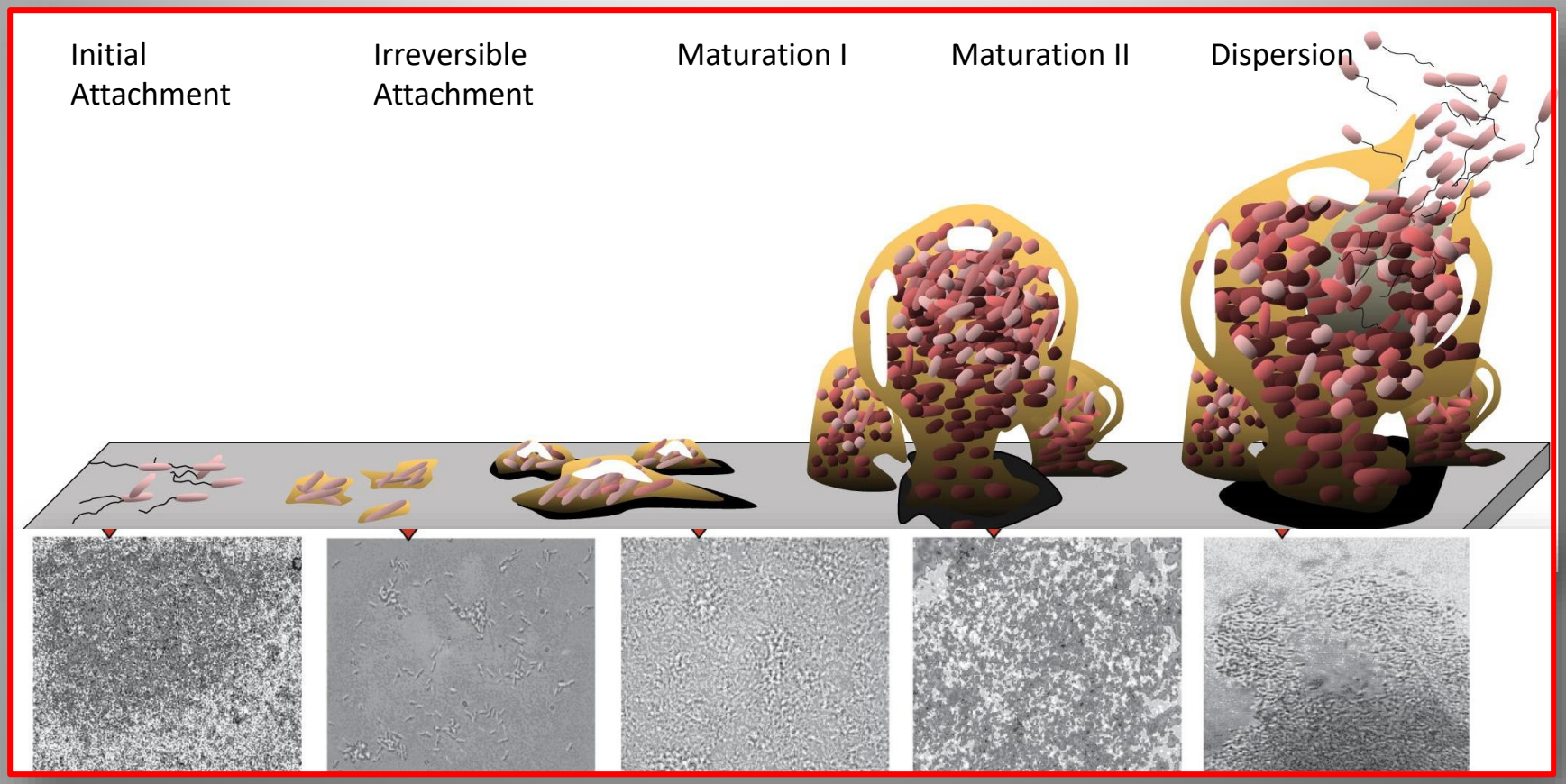
(Christensen, 2009)

Biofilms

- Aggregate of microorganisms adherent to each other or a surface
- Embedded in a self-produced matrix of extracellular polymeric substance
- Cells in a biofilm are physiologically distinct from planktonic cells
- Biofilm growth mode causes large shift in gene regulation
- Increased resistance to antibiotics & detergents



Bioflim Formation & Cycle



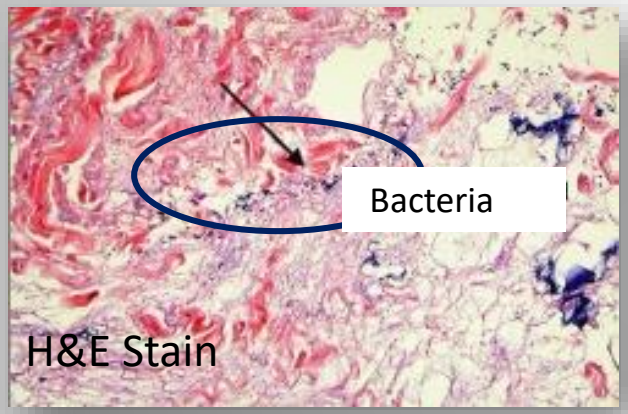
Bioflim Infection Challenges

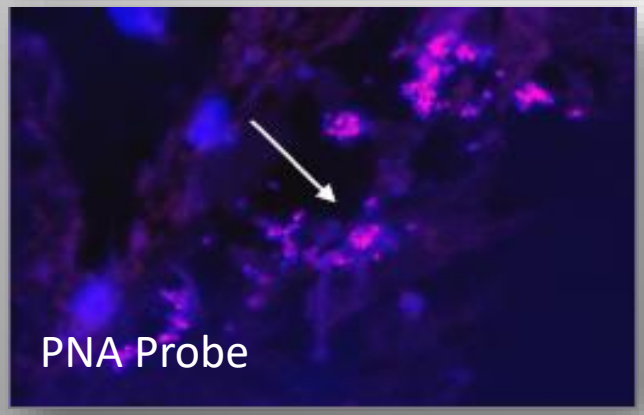
- Increased antibiotic resistance (1000x drug needed)
- Leucocytes trapped & made ineffective
- Chemical communication promotes bacterial cooperation
- Dormant (persister) cells have decreased metabolism
  - Difficult to culture
  - Resistant to antibiotics
- Clinical failure to recognize infections
- **RESULT: Low-grade smoldering infection**
  - **Low host response**
  - **High antibiotic resistance**
  - **Low possibility of positive culture**

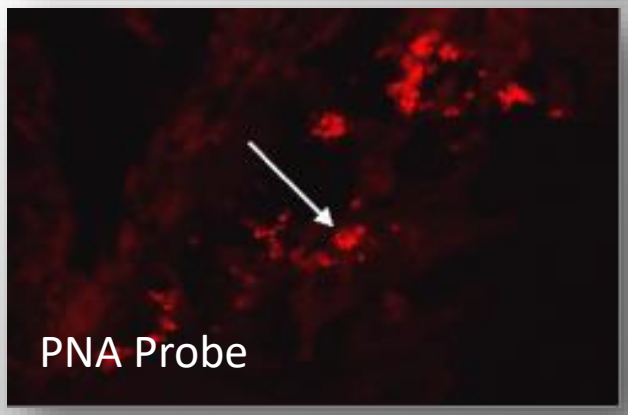
Bioflim Detection

- Biofilm detection requires fluorescent DNA stains or other chemical reactions
- May need 4 to 6 weeks on specific agar plates

Bacteria in Gel







Bjarnsholt 2009

Fillers Susceptible to Biofilm Complications

Combination Gels (more likely)

- Collagen–PMMA suspensions (Artecoll)
- HA–PMMA suspensions (Dermalive ,Dermadeep, Dermatech)
- Bioplastique (silicone in polyvinylpyrrolidone)
- Evolution (polyacrylamideco-DADMA)
- Bio-Alcamid (polyalkylmide)
- Outline (procollagen)

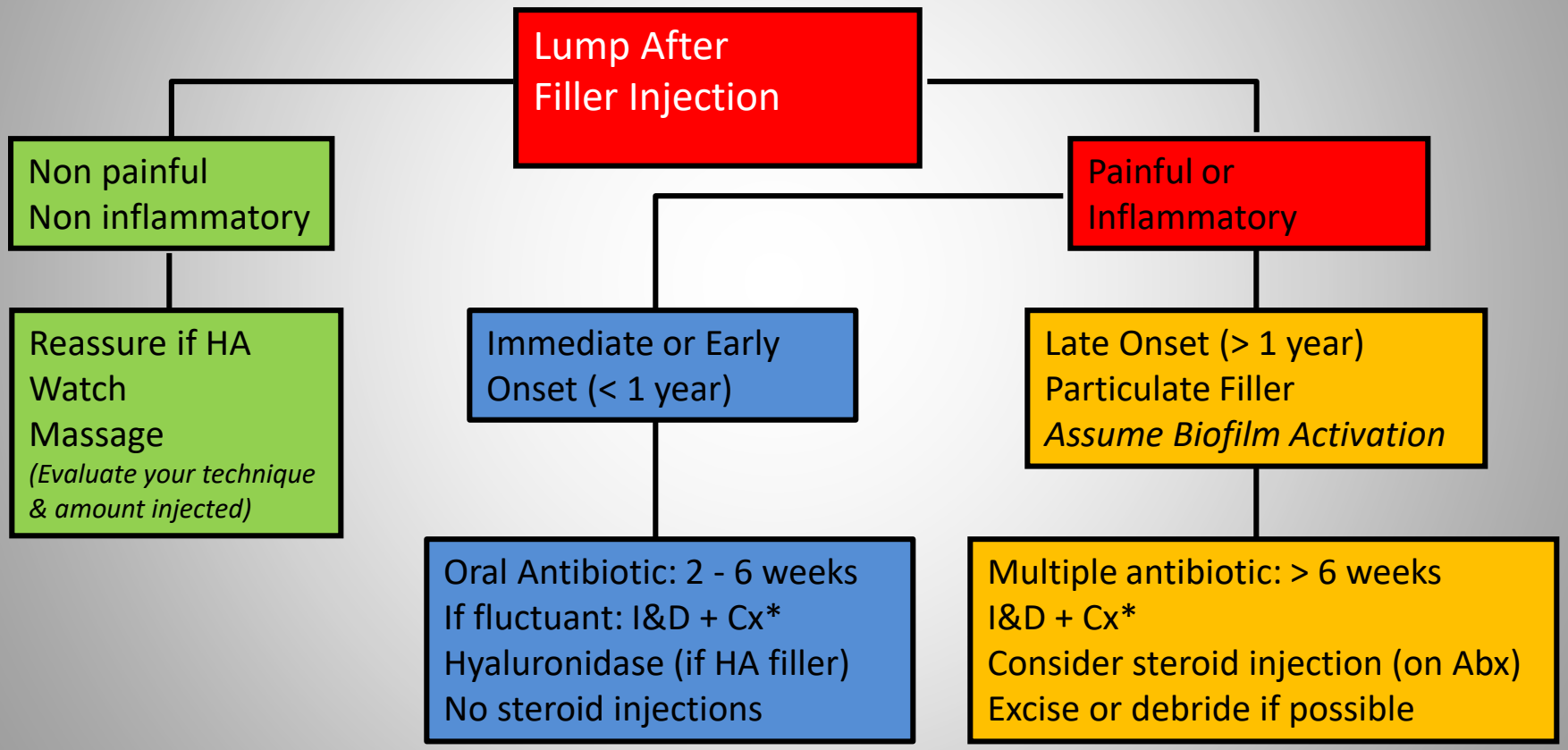
Homogenous Products (less likely)

- Radiesse
- Silicone
- Polyacrylamides

Biofilm 2 Week Window

- 2-week period after implant placement when bacterial contamination can occur and develop a biofilm
- Timeline documented in orthopedic implants & other solid foreign body implanted material
- Avoid needle injections over the implant during the 2 weeks
- Dental procedures, facial trauma, or facial infections can introduce bacteria and produce biofilm

Treatment Algorithm



Antibiotic Treatment

Most Early Infections

- Clarithromycin 500 mg BID x 6 weeks
- Minocycline 100mg BID x 6 weeks

Recurrent infections suggest active biofilm

- Filler & biofilm must be removed/excised

Laser Treatment of Filler Lesions

- Infectious lesions
  - 532 nm lithium triborate laser
  - Removal of infected gel & pus
- Granulomas
  - 808 nm diode laser (intralesional technique)
  - Melt & liquefied then granuloma
  - Facilitates evacuation
- Thin laser beam
  - Controlled tissue
- 20 patients had reduction or complete resolution
  - Resolution increased with repeated treatments
  - All had prior antibiotics & steroids without success

Cassuto 2009

Laser Treatment of Filler Lesions

- Cystic lumps 3 months after HA & dextranomer microsphere injections
- 6 weeks antibiotics & steroids no resolution
- Multiple 532 nm lithium triborate laser treatments

Cassuto 2009

Laser Treatment of Filler Lesions

- Granulomas after Dermalive* & Aquamid**
- 808 nm diode laser treatment
- Drill holes for evacuation

* HA + acrylic hydrogel
** Polyacrylamide

Cassuto 2009

FDA Safety Communication

Signs & Symptoms of Intraarterial Injection

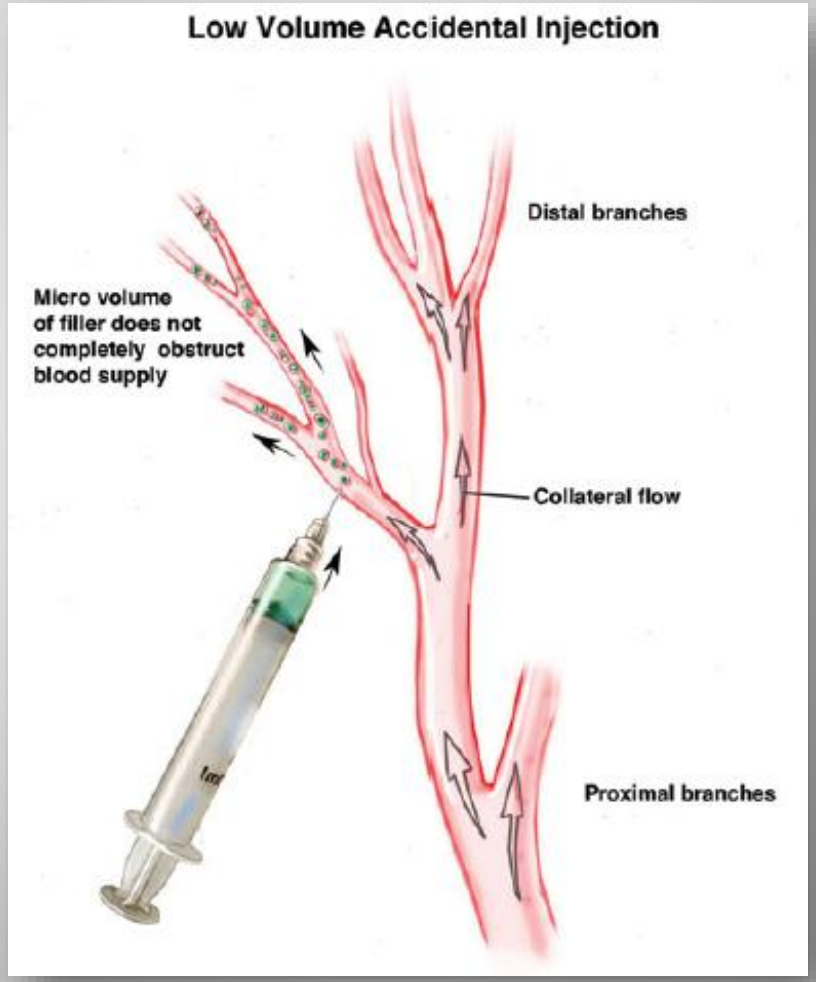
- Skin
  - Pain
  - Nausea
  - Skin blanching
  - Slow capillary refill
  - Demarcation
- Eye
  - Vision loss/blindness
- Stroke
  - “FAST”: facial drooping, arm weakness, speech impediment, time (act fast!)

Progression of Skin Changes

Findings	Timing
Blanching	Seconds
Reactive hyperemia or livedo pattern	Minutes up to 10 minutes
Blue-black discoloration	10 minutes to hours
Blister/bullae formation	Hours to days
Skin breakdown, ulceration, slough	Days to weeks

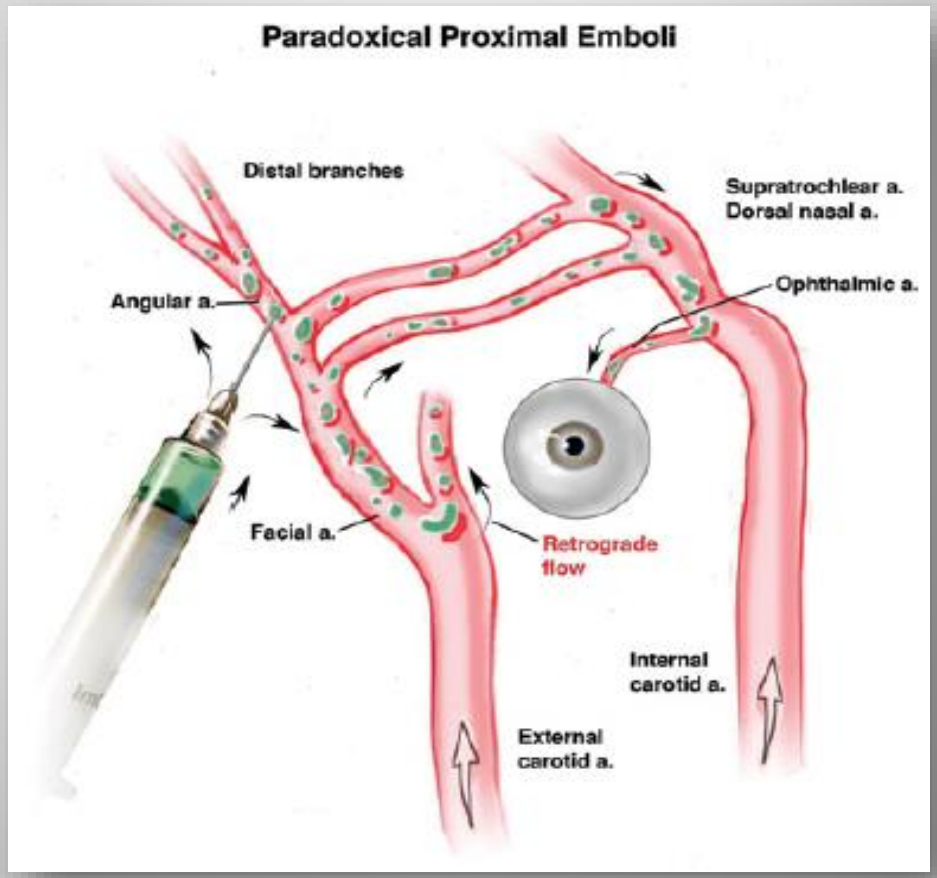
DeLorenzi C. Complications of injectable fillers, Part 2: Vascular Complications. ASJ. 2014.

Low Volume Injection & Arterial Occlusion



DeLorenzi C. Complications of injectable fillers, Part 2: Vascular Complications. ASJ. 2014.

High Injection Pressure & Retrograde Propagation

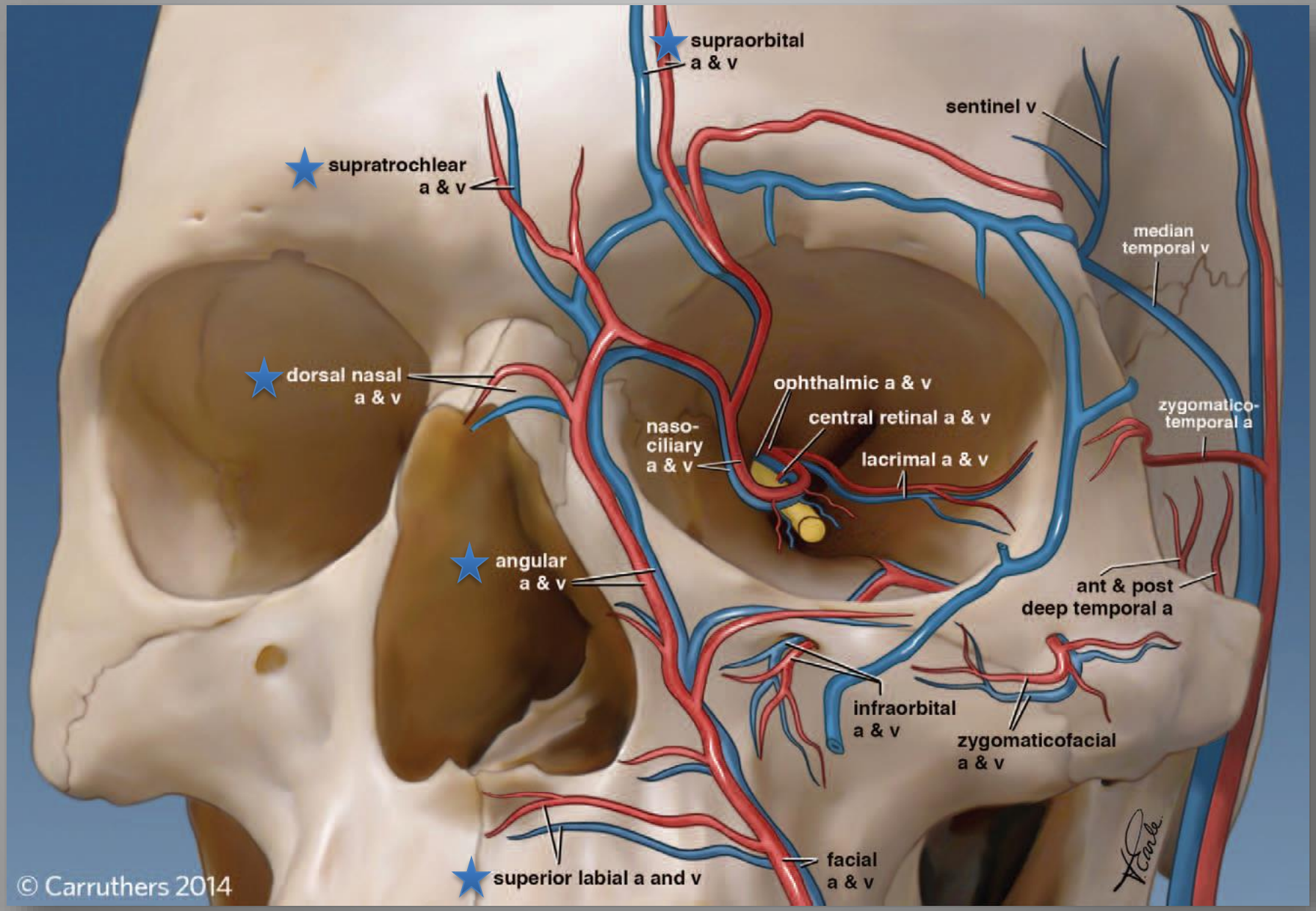


DeLorenzi C. Complications of injectable fillers, Part 2: Vascular Complications. ASJ. 2014.

Avoid Arterial Injection & Propagation

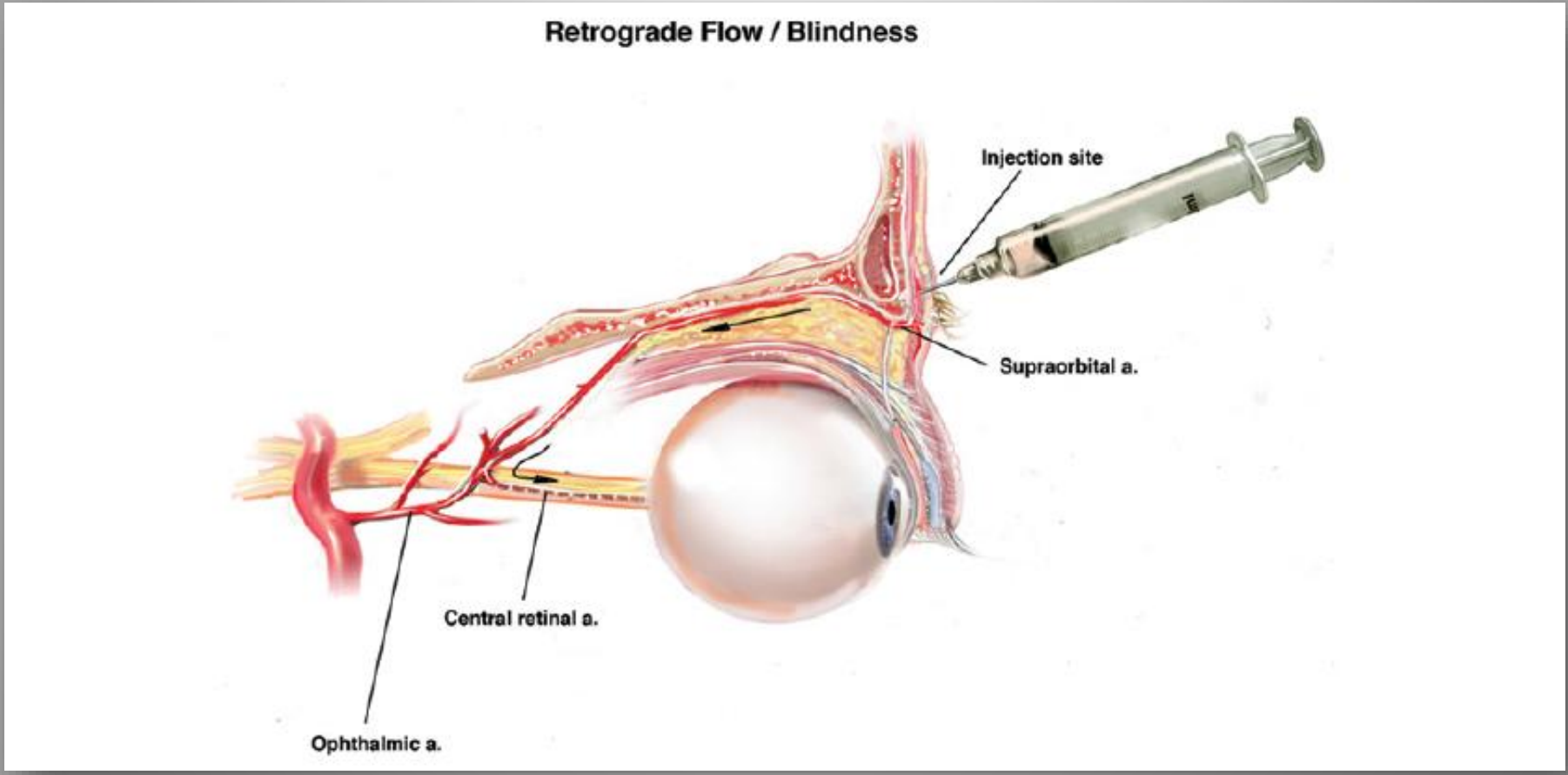
- Withdraw before injection
- Avoid deep injection near named vessels
- Low pressure injection
- Avoiding injecting excess volume in one area
- Blunt cannulas
- Small bore
- Inject slowly in small aliquots
- Avoid injection in previously traumatized areas
- Stop injection if complaints of pain/vision loss

Carruthers JDA, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler injection: a review of cause and therapy. PRS. 2015.



Carruthers JDA, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler injection: a review of cause and therapy. PRS. 2015.

Blindness



DeLorenzi C. Complications of injectable fillers, Part 2: Vascular Complications. ASJ. 2014.

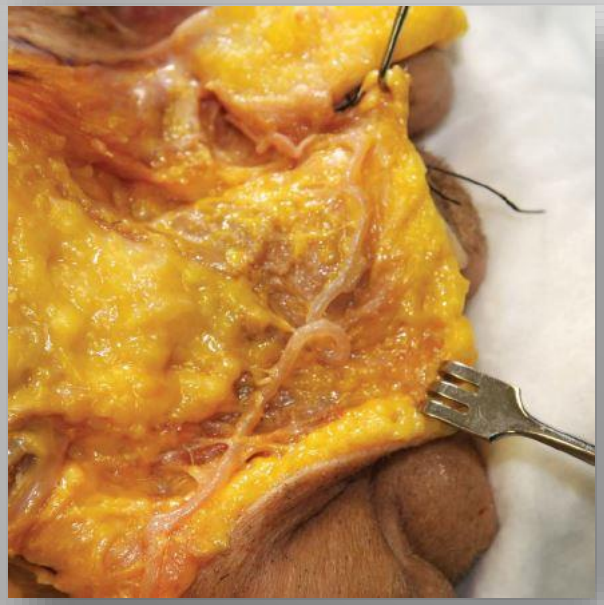
Crash Kit

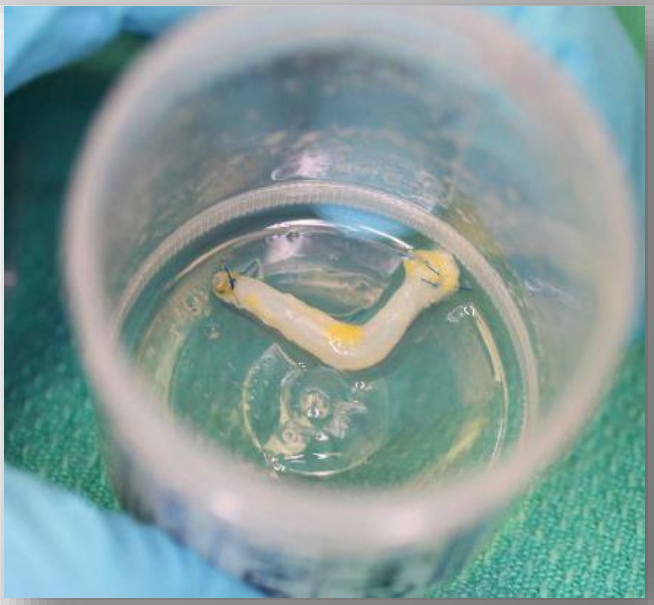
- Warm compress
- Nitropaste
- Baby ASA
- Supplemental O2
- HYALURONIDASE
  - 400U into subcutaneous area (2cc in a 3cc syringe with 0.2cc plain lidocaine 2%, 27 g-needle)

Hyaluronidase

Transarterial Degradation of Hyaluronic Acid Filler by Hyaluronidase

Claudio DeLorenzi, BA, MD, FRCS





Intravascular HA liquefied in cadaver arteries &veins after 4 hours

Hyaluronidase

Hyaluronidase works for

Juvederm

Ultra & Ultra Plus

Voluma & Volbella

Restylane

Lyft & Silk

Belotero

Always have Hylenex available when doing HA injections

Filler Emergencies

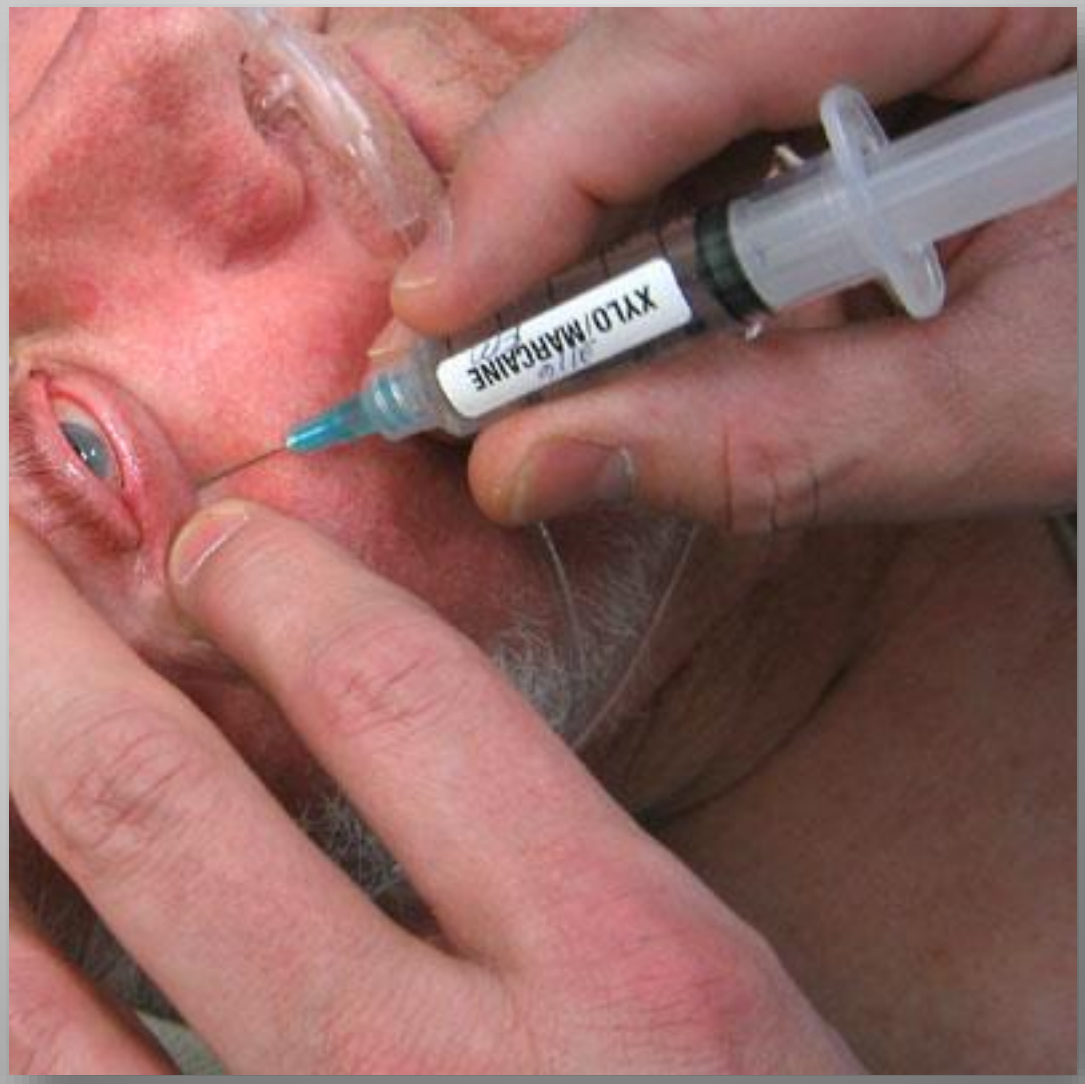
- Soft tissue intravascular occlusion
- Stroke
  - Standard emergency stroke protocol
- Vision loss/blindness
  - Emergency ophthalmology consult
  - Retrobulbar hyluronidase injection

Retrobulbar Injection Technique

- Local anesthesia into lower eyelid over inferotemporal orbit
- Blunt, 25g cannula advanced in inferotemporal quadrant of orbit for 1 inch
  - Inferior and lateral to optic nerve
- 2 to 4cc hyaluronidase

Carruthers JDA, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler injection: a review of cause and therapy. PRS. 2015.

Retrobulbar Injection Technique



Complications

Posted on Real Self

Use Informed Consent Forms!

Filler Complications

- All fillers have potential complications
- Long lasting
  - More persistent
  - More difficult to treat
- Complications due to technique vs material
  - Learn technique on temporary fillers
  - Experience decreases technique complications

Recommendations

- Know the filler material you are using
- Start with temporary & reversible products
  - Hyaluronic acids
- Use sterile techniques
- Limit amount injected & areas treated
  - Easier to add than to take away
- Deal with inflammatory nodules
- Know the regulatory issues

Regulatory Issues

Fillers & the Law

- Product purchase source
- Non-FDA approved fillers
- Patient supplied fillers
- Off label filler use
- Reimporting FDA approved fillers
- Physician vs non-physician filler injector
- Non-clinical treatment settings

Purchase Directly from Manufacturer

5 Docs Plead Guilty in Bogus Botox Rap; Stems From Toxin Research International Case

By Jim Edwards | Aug 14, 2009

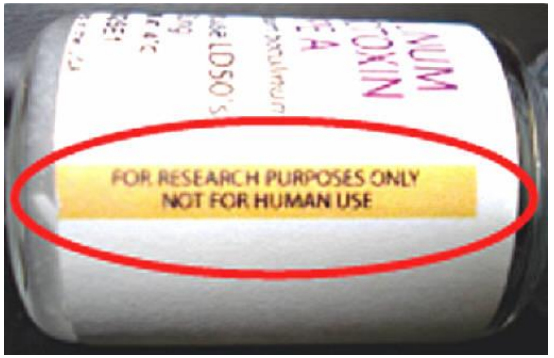
Five prominent New York State doctors pled guilty this week to injecting patients with an unapproved version of **Botox**, and not telling those patients they weren't getting the real thing. They face a possible year in prison and a $100,000 fine on a misdemeanor misbranded drugs charge.

The doctors bought the Botox from **Toxin Research International** in Arizona. The doctors maintain they thought it was the real thing, and no patients were injured.

The president of Toxin Research International is currently serving nine years in prison for fraudulently selling misbranded Botox on the web.

The case is a warning to doctors: get your supplies through established channels, not the secondary market.

These weren't sleazy docs operating out of strip malls. Their resumes read like pillars of the community.



Non FDA Approved Fillers

Is it legal for a physician to obtain and use a product from outside of the United States that is <u>not approved by the FDA</u>?

- An individual who enters the country with a non-approved injectable filler could be sanctioned by the FDA
- A physician who orders a non-approved injectable filler through a non-US mail-order pharmacy could be sanctioned by the FDA
- State medical board involvement if any patient complaints result
- Exceptions for investigators working under FDA-approved studis

Patient Provided Fillers

If a patient brings a non-approved drug or device to a physician, is it legal to treat the patient using this drug or device?

- Federal law prohibits such conduct
- Risk of significant liability exposure, invalidation of professional liability insurance coverage, criminal penalties and action by regulatory agencies

ASPS & ASAPS 2006

Off-Label Filler Use

What is the risk exposure of off-label use of approved drugs?

- Off-label use of FDA approved drugs does **not** carry the risks cited above, provided patient acceptance and understanding, and the treatment rationale, are well documented
- For example, Botulinum toxin type A is a FDA-approved product for use in the glabellar area. Use of the product in other areas is legal and a clinical decision

Can a physician advertise non-approved or off-label use?

- It is illegal to commercially advertise any non-approved or off-label use; only FDA-approved uses may be commercially advertised

Reimported Fillers

Is it legal for a physician to purchase and use an FDA approved drug/product that is reimported from foreign sources?

- The act of importing drugs manufactured or approved in the U.S. and approved by the FDA is called “reimportation”…which remains illegal and dangerous
- Currently, only manufacturers are allowed to reimport their own drugs

ASPS & ASAPS 2006

Non-Physician Filler Administration

What level of training or licensure is required to administer injectables or fillers?

- Injections may be administered by a licensed professional nurse or physician assistant as determined by the supervising physician & local and state professional practice regulations
- Physician's responsibility to ensure the non-physician possess proper education and training

What are the legal requirements for physician supervision of non-physician personnel who administer injectables and fillers?

- Supervisory regulations vary from state to state
- Physician of record is ultimately responsible

ASPS & ASAPS 2006

Non-Clinical Treatment Settings

- **Administration of injectables & fillers outside a clinical setting**
- Concern about non-clinical sites where treatments offered
  - Shopping malls, private homes, office parties, and group social gatherings
- Inappropriate for several reasons:
  - Inadequate patient selection
  - Possible peer pressure for an individual to consent to treatment
  - Providers who are not trained or qualified to treat or deal with complications
  - Lack of control over dosage and inadequate post-treatment supervision
  - Alcohol influencing decision making
  - Dealing with adverse event

Update In Process

PMMA Filler for Treating Acne Scars

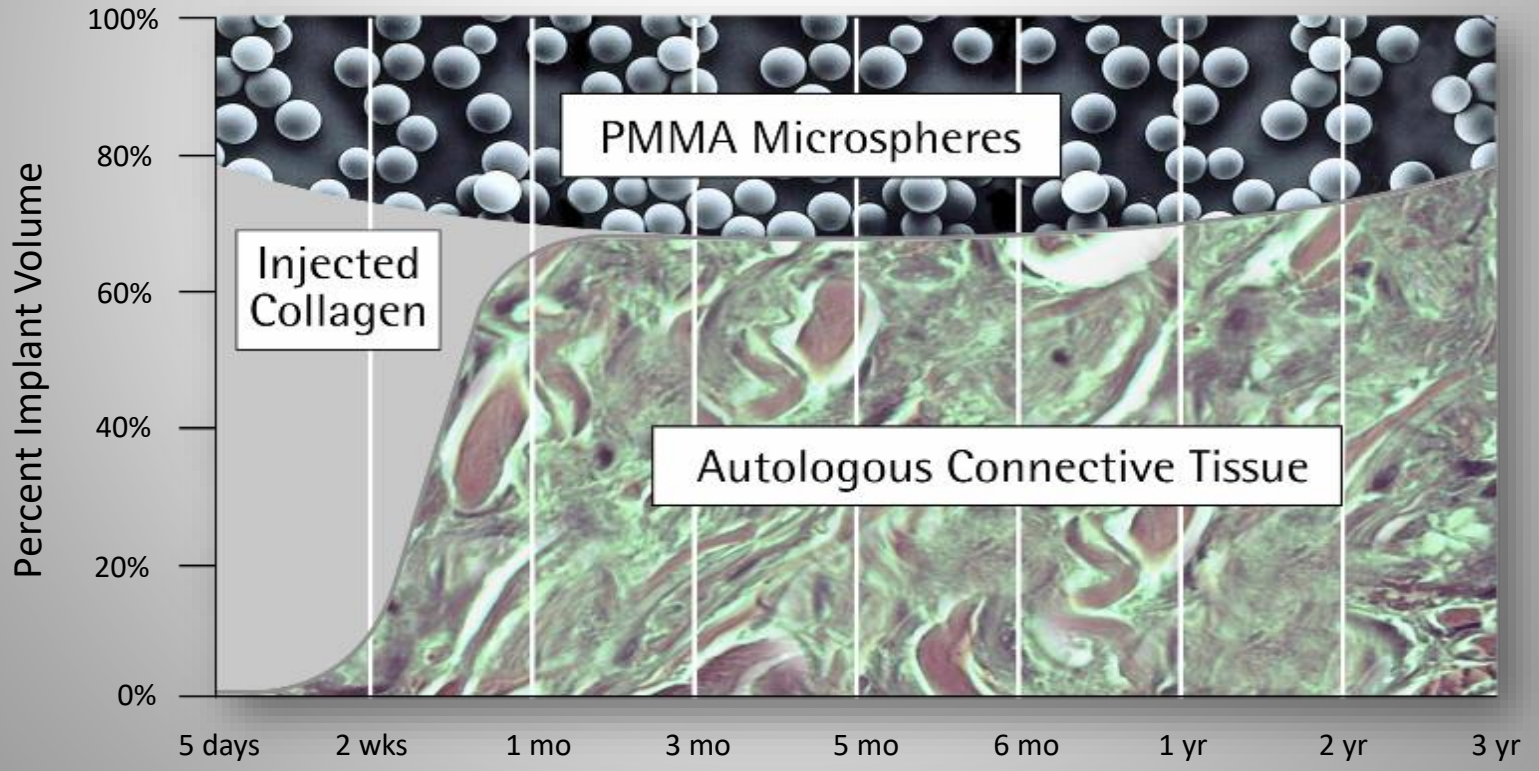
Karol A Gutowski, MD, FACS

Acne Scar Treatment Options

- Fillers (HA, PLLA)
- Laser resurfacing
- Chemical peels
- Topical treatments
- Dermabrasion
- Subcision
- Excision

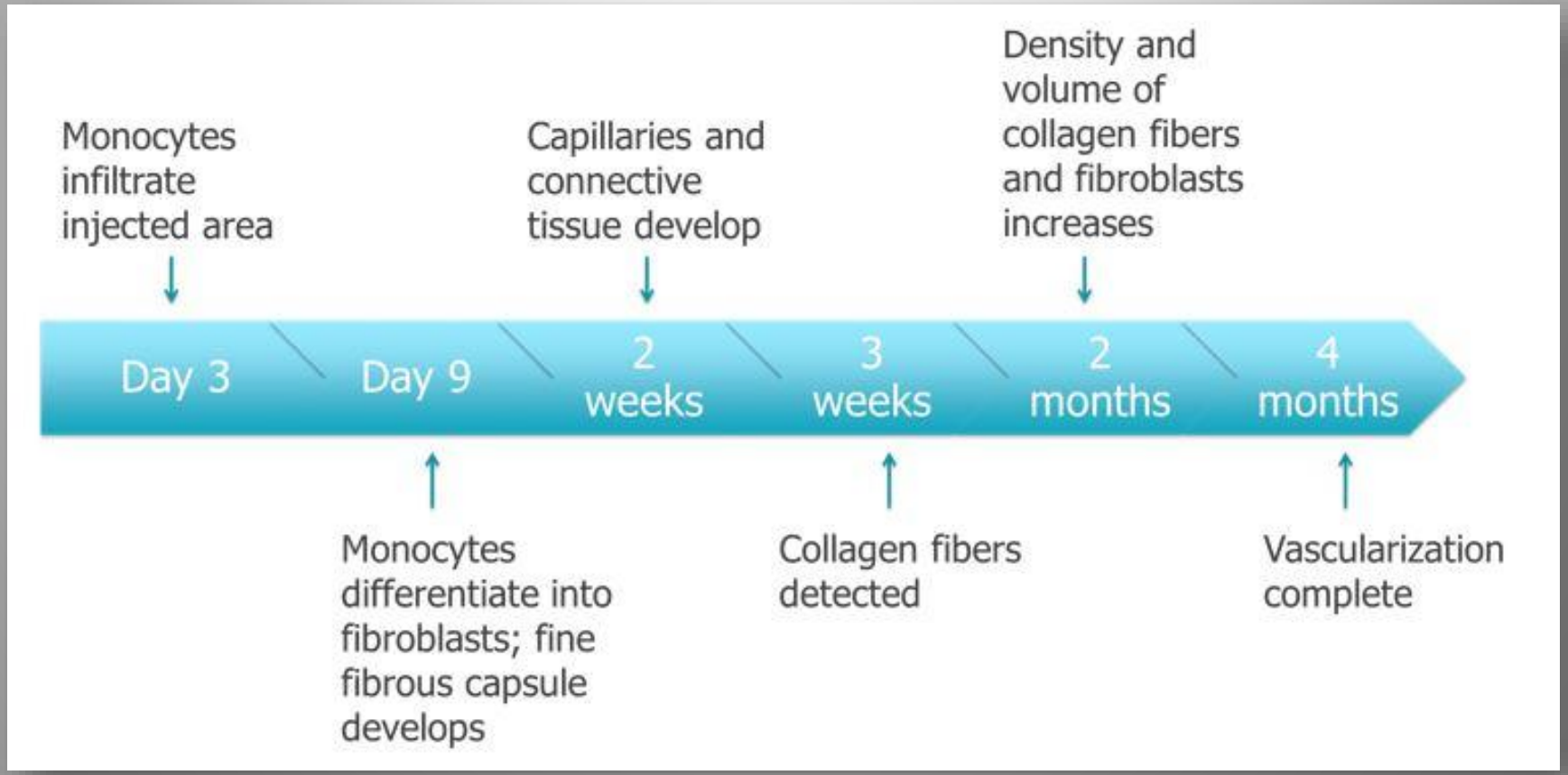
Bellafill Mechanism of Action

- Initial volumization (bovine collagen)
- Secondary autologous collagen stimulation (PMMA)



Time Line

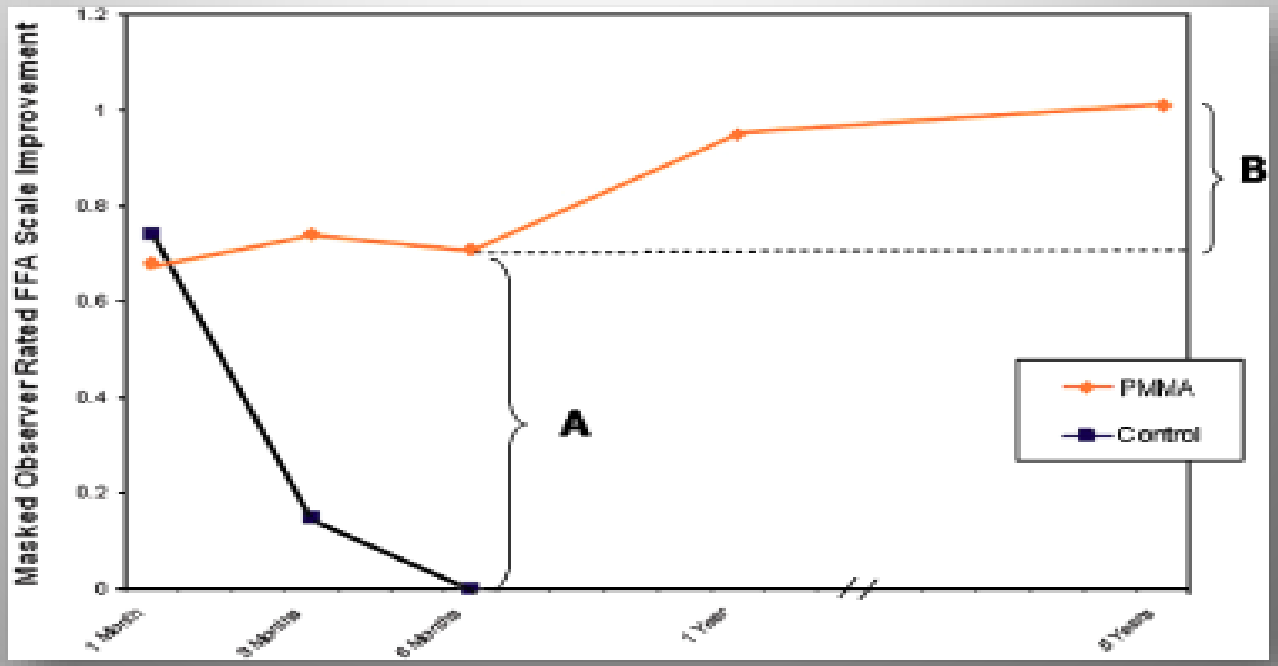
6 to 8 weeks to final result



Update on Duration of Effect

Post Marketing Study

- 145 patients followed for 5 years
- 5 year 90% patient & investigator satisfaction



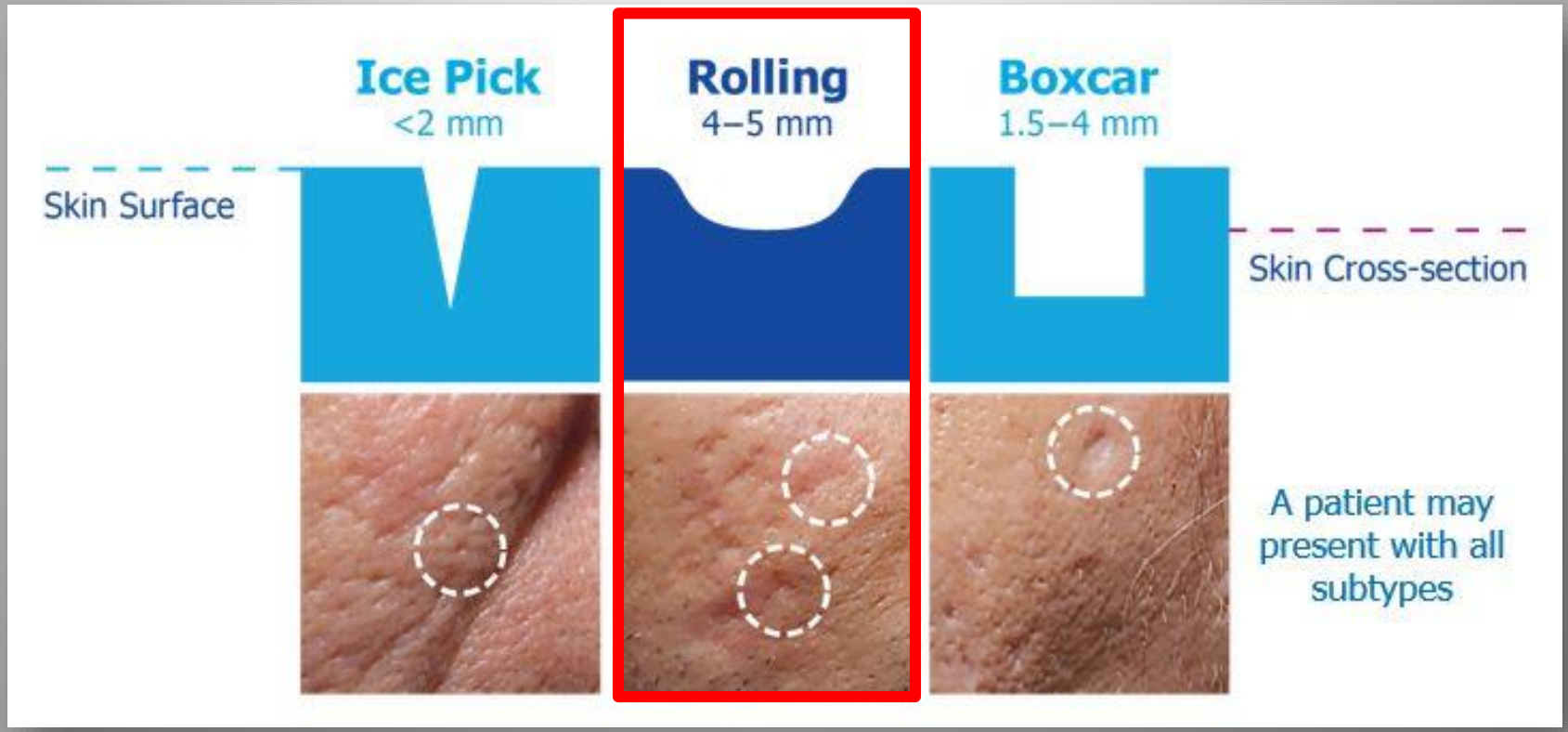
Update on Duration of Effect

5 Year Safety Trial

- 1008 patients followed for 5 years
- 87% retention
- 94% “somewhat” to “very satisfied”

Atrophic Acne Scars

Rolling scars improved with <u>skin traction</u>



Bellafill FDA Approved for Acne Scars

Scars Improved with Traction

Acne Scar Assessment

Category	Score	Description
Minimal	1	Depth up to .5 mm
		Visibility = Perceptible with tangential lighting
Mild	2	Depth >.5 mm to <1.5 mm
		Visibility = Moderately detectable with tangential lighting
Moderate	3	Depth ≥ 1.5 mm to <2.5 mm
		Visibility = Easily seen with tangential lighting
Severe	4	Depth ≥ 2.5 mm
		Visibility = Substantial shadowing with tangential lighting

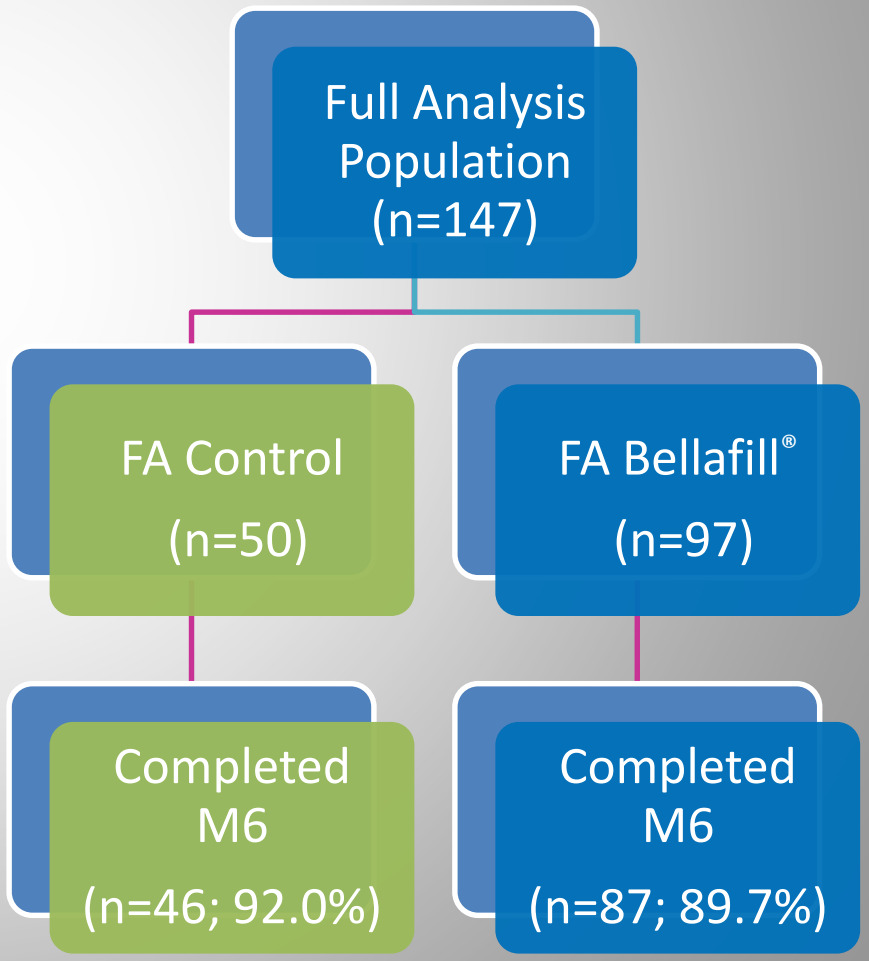
Study: Grade 3 & 4 rolling acne scars

Patient Selection

Study: Grade 3 & 4 rolling acne scars

ERAS Trial

- Double blinded RCT at 10 sites
- Mean age 45 yo, 2/3 female
- Average 0.1 cc per scar
  - 1.0 cc first treatment
  - 0.7 cc touch up treatment
- 80% touch up treatment
- Effectiveness: At least 50% of scars improved by ≥2 points (4 point scale) at 1 year



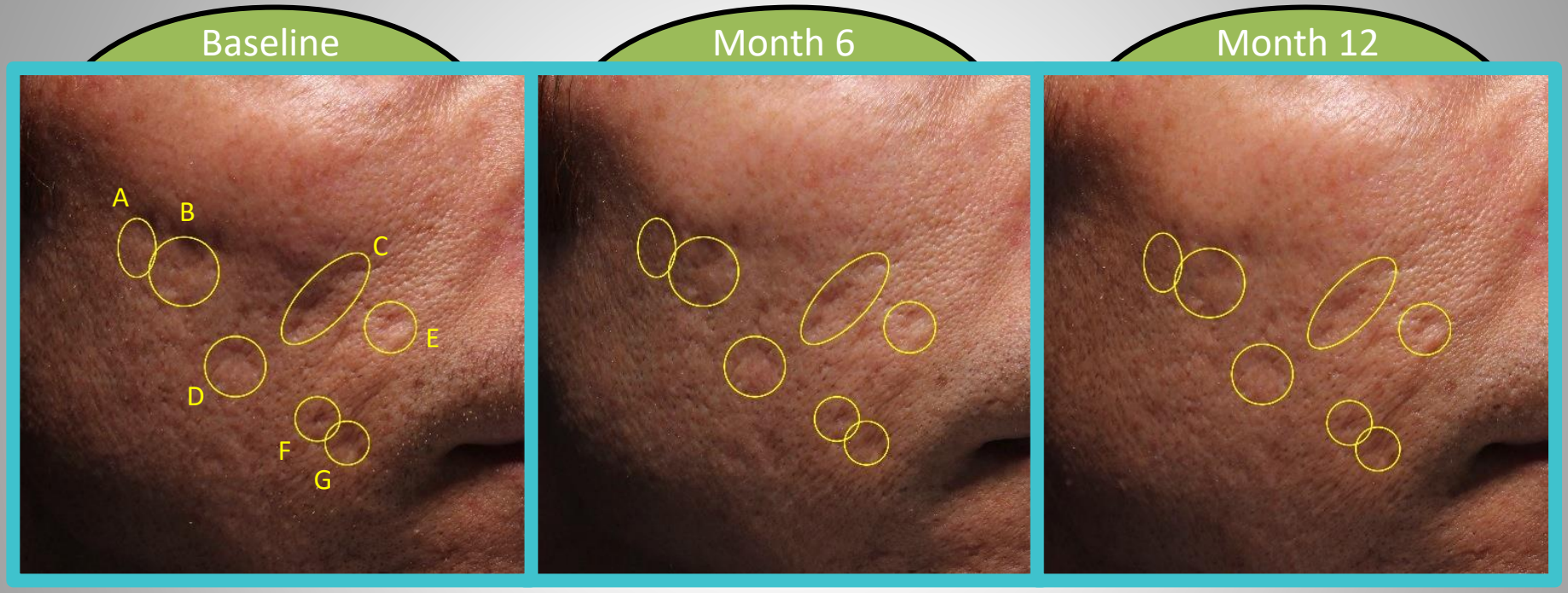
ERAS Trial: Investigator Evaluation

ERAS Trial: Adverse Events

Reported in > 1% of subjects

Adverse Events, n (%)	PMMA-collagen n = 143*	Control n = 50
• Injection site reaction—lumpiness and papule (3 mild, 1 moderate)	4 (2.8%)	0 (0)
• Injection site bruising (2 mild, 1 severe)	3 (2.1%)	0 (0)
• Injection site pain (mild)	3 (2.1%)	0 (0)

Results



2 syringes over 2 treatment sessions total for both cheeks

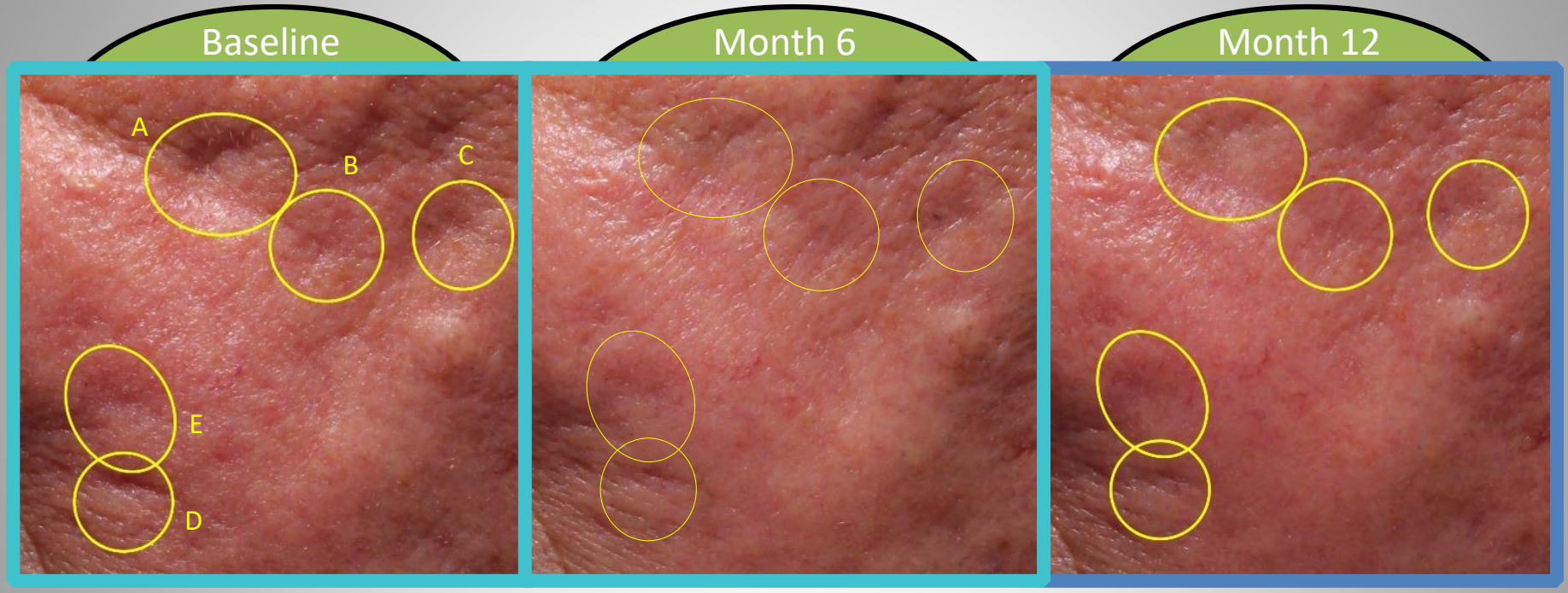
Only circled scars were treated

Results

2 syringes over 2 treatment sessions total for both cheeks

Only circled scars were treated

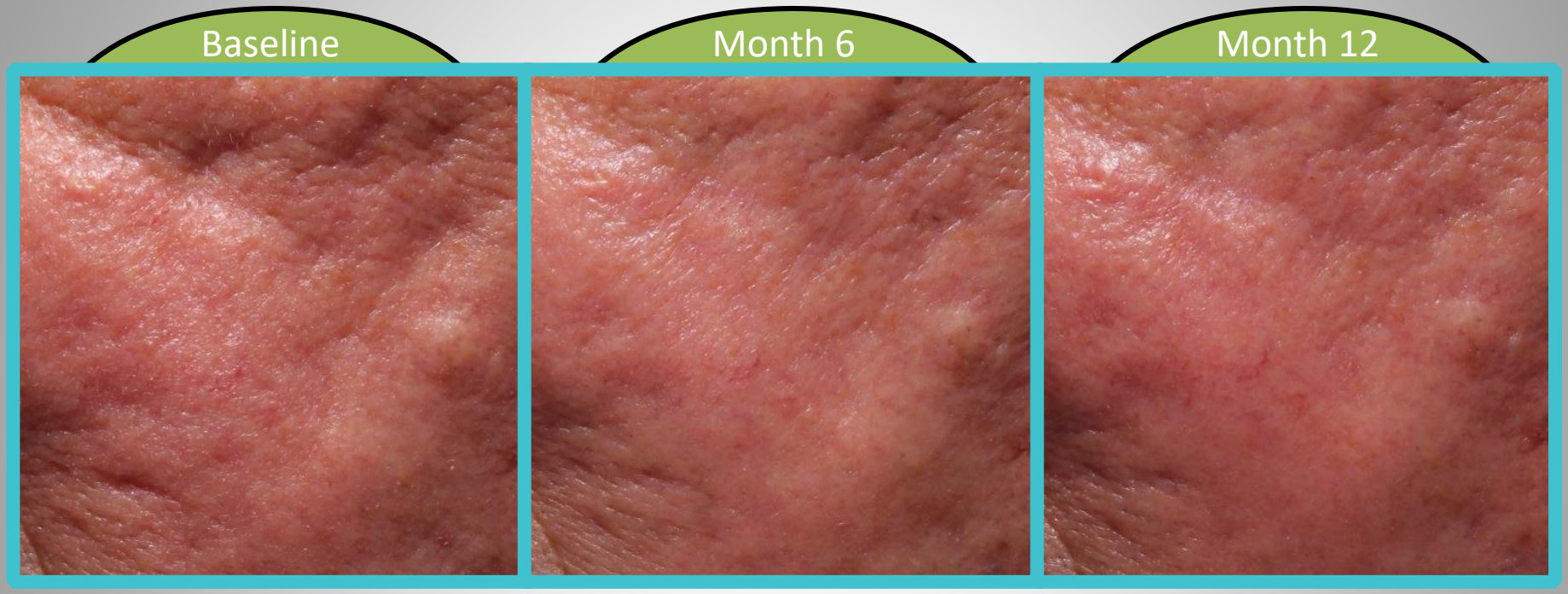
Results



2.5 syringes for each cheek

Only circled scars were treated

Results



2.5 syringes for each cheek

Only circled scars were treated

Results

Only circled scars were treated

Results

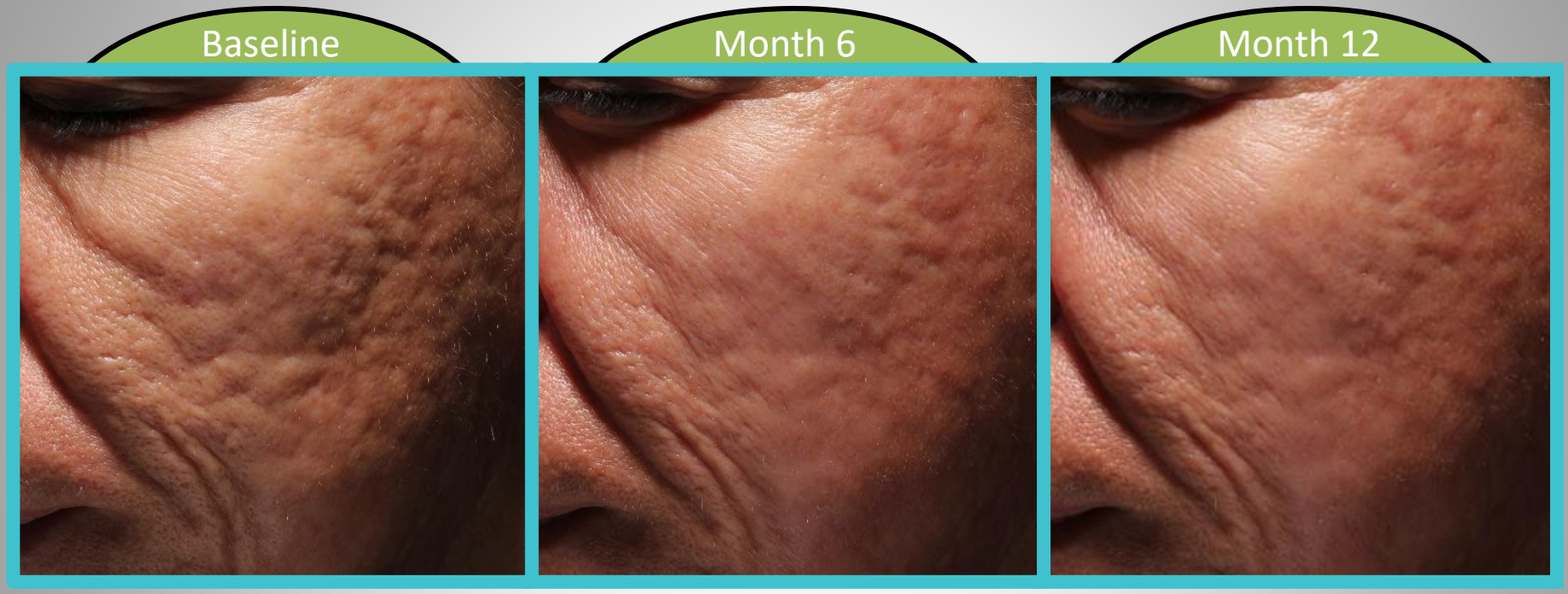
Only circled scars were treated

Results

0.4 cc for these 3 sites

Only circled scars were treated

Results



0.4 cc for these 3 sites

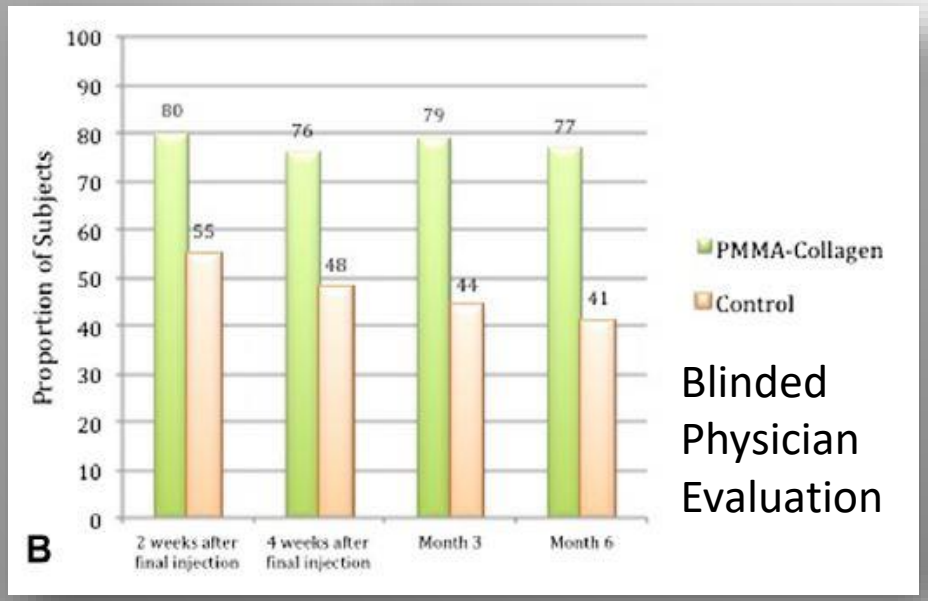
Only circled scars were treated

Independent Study

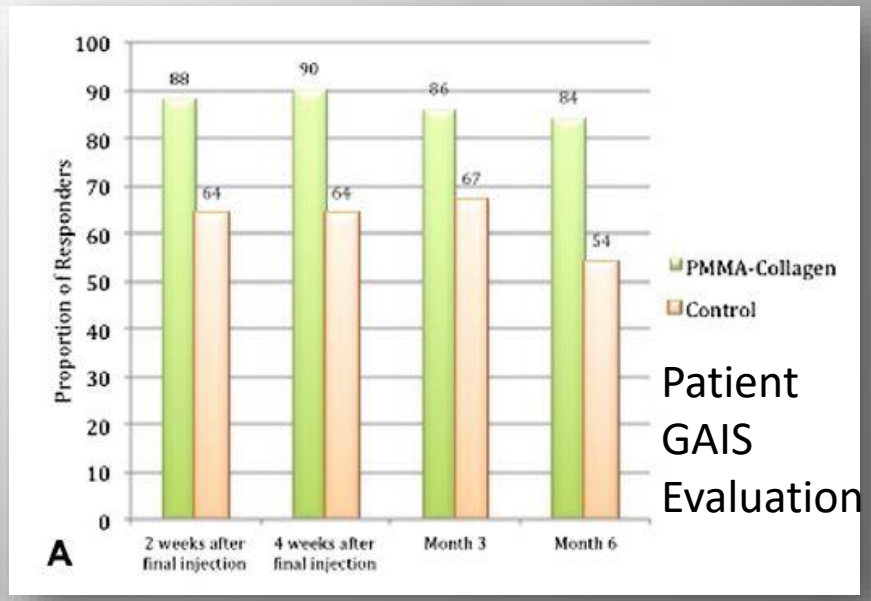
A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars

Jwala Karnik, MD,[a] Leslie Baumann, MD,[l] Suzanne Bruce, MD,[b] Valerie Callender, MD,[c,d] Steven Cohen, MD,[e,f] Pearl Grimes, MD,[m] John Joseph, MD,[h] Ava Shamban, MD,[i] James Spencer, MD,[j] Ruth Tedaldi, MD,[n] William Philip Werschler, MD,[k] and Stacy R. Smith, MD[g]
Santa Barbara, San Diego, Beverly Hills, and Los Angeles, California; Miami, Florida; Houston, Texas; Glenn Dale, Maryland; Washington, District of Columbia; New York, New York; Wellesley, Massachusetts; and Seattle, Washington

2014



Blinded Physician Evaluation



Patient GAIS Evaluation

Personal Experience

- Challenges with photo documentation
  - VISIA not useful
- Patient expectations
  - Moderate to severe rolling scars
- Multimodality approach
  - Micro-needling
  - Chemical peels
  - Fractional CO2 laser

Injectable Soft Tissue Fillers: Practical Applications

Karol A Gutowski, MD, FACS

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