



Stanford
University

Optical imaging and quantification of microvascular systems in plastic and reconstructive surgery

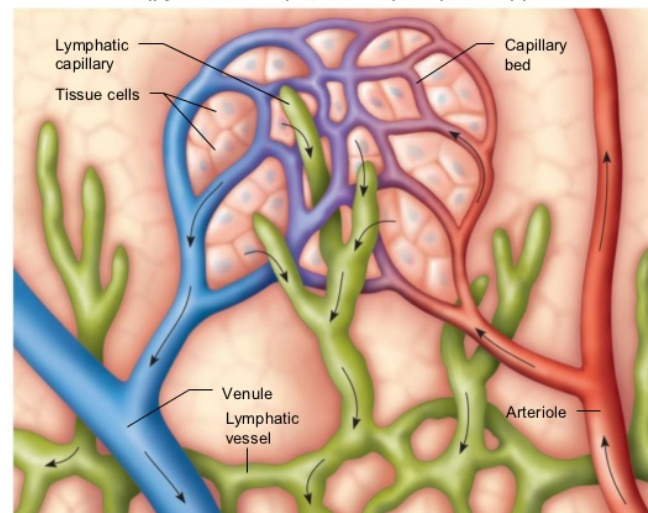
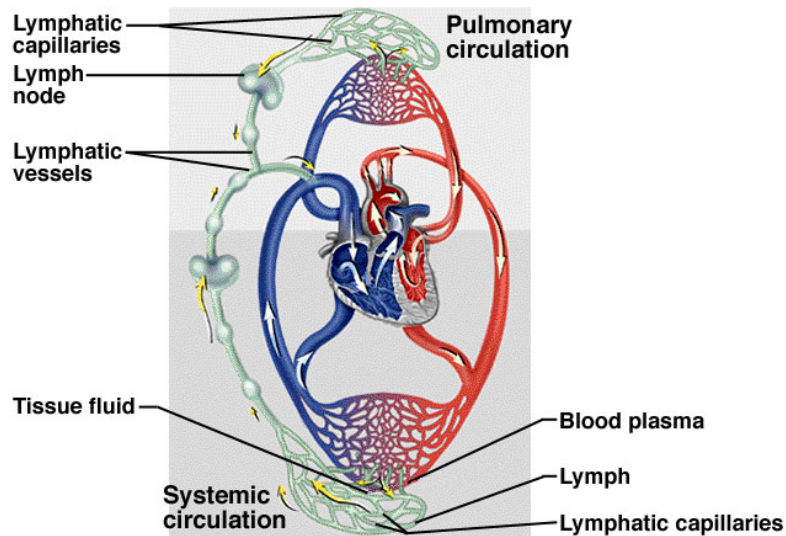
Siavash Yousefi, PhD

Department of Radiation Oncology,
Stanford University,
Stanford, CA



Microcirculatory Network

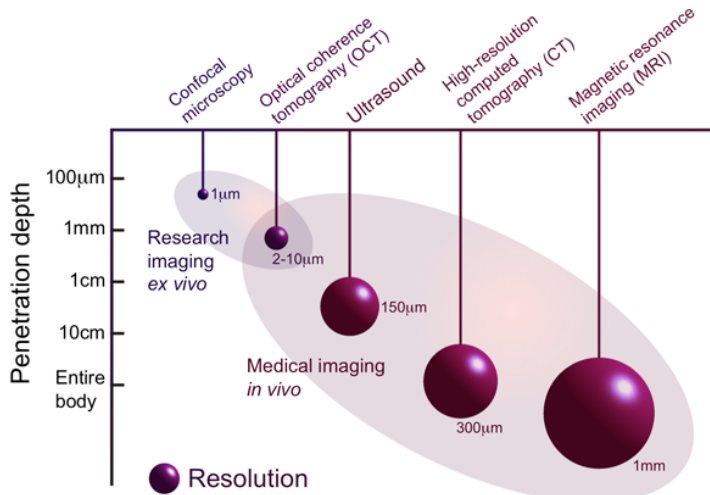
- Circulatory network: Cardiovascular and lymphatic system
- Deliver oxygen, nutrition, immune cells and hormones to tissue via **arteries** and collects waste materials from cells via **veins** and **lymphatic** vessels.
- Exchanged with cells via **capillary beds**.



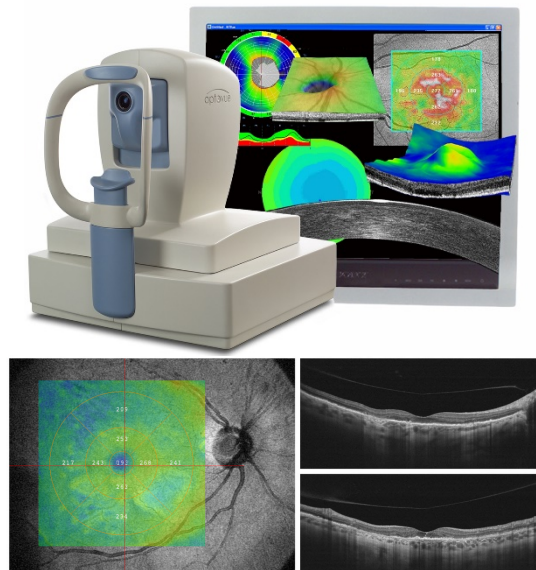
Optical coherence tomography (OCT)

- A non-contact, non-invasive, depth-resolved, 3D, biomedical image modality capable of producing high-resolution ($\sim\mu\text{m}$) cross-sectional images of optical scattering media

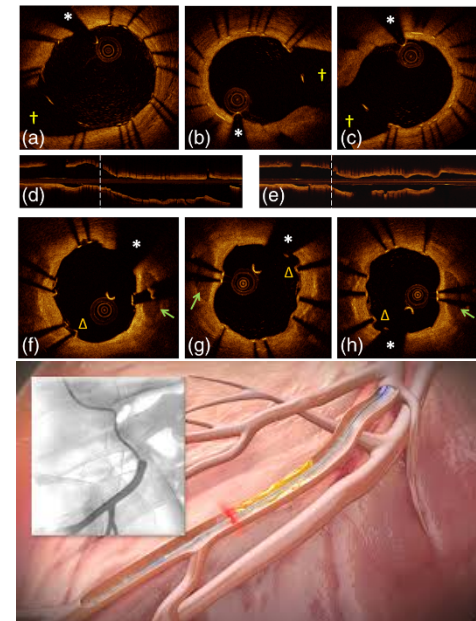
Depth-resolution comparison



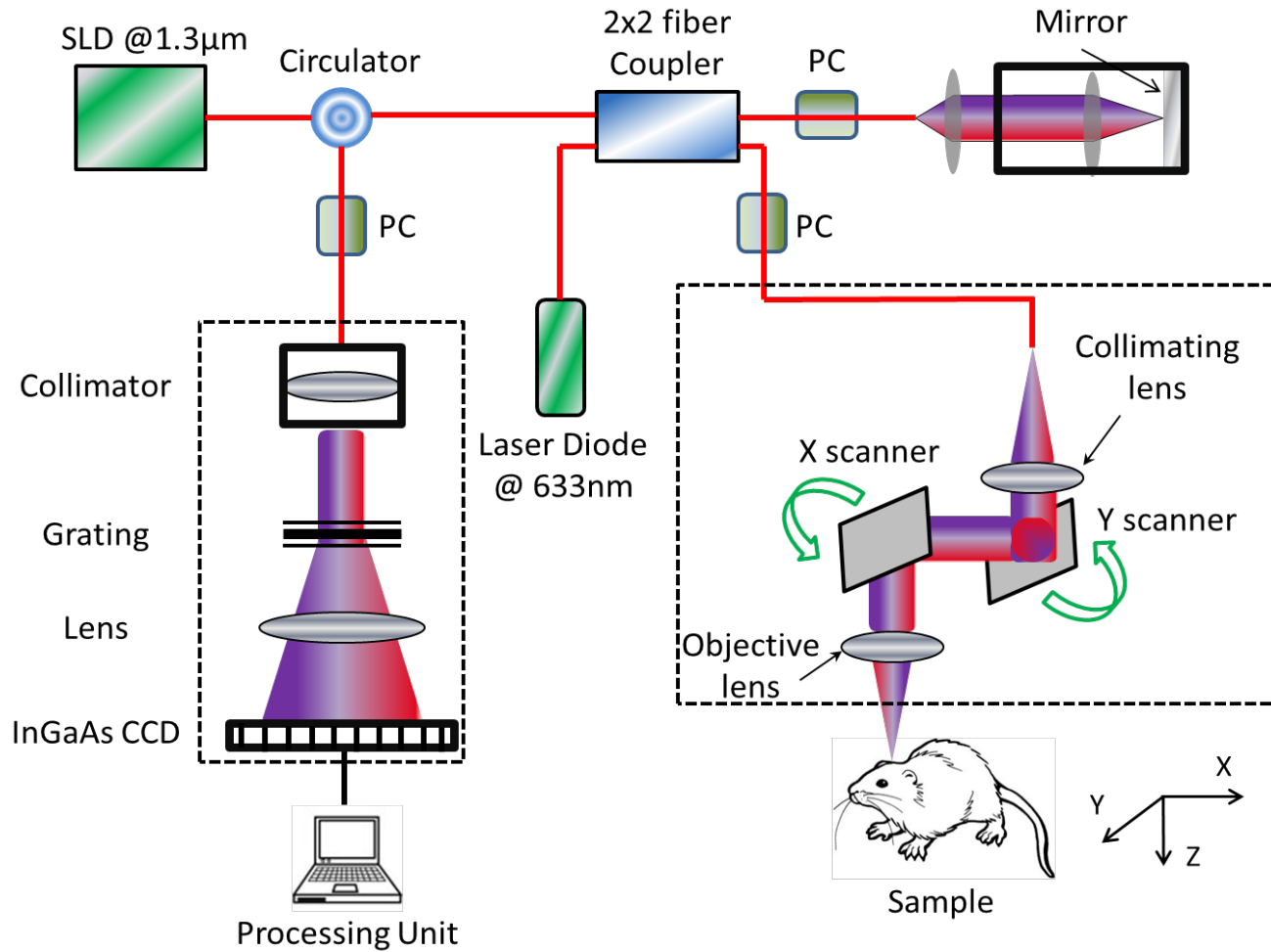
Ophthalmology



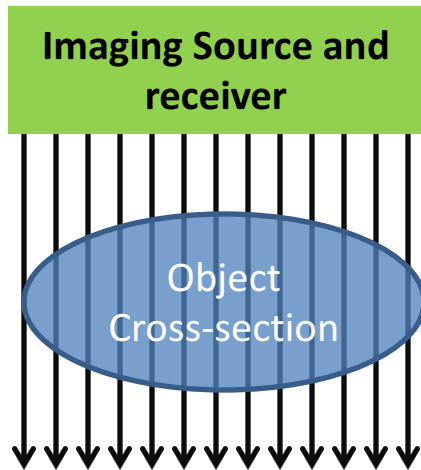
Intravascular Cardiology



OCT System Set-up

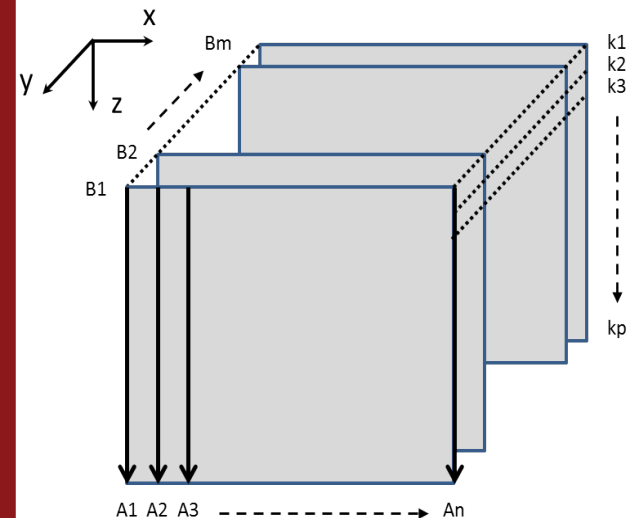


OCT 3D Image Formation



Each measurement along the depth (z) is called an **A-line**

By scanning the beam along the fast scan direction (x) and placing adjacent A-lines, a **B-scan** (tomogram) is formed

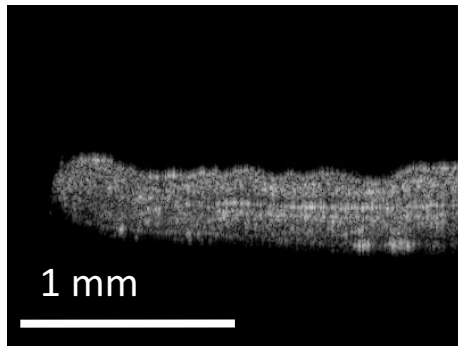


By scanning along the slow scan direction (y) and acquiring B-scans and placing them next to each other, a **3D OCT** image is formed.

Optical Micro-Angiography (OMAG)

- **OMAG:** 3-D dynamic blood perfusion within microcirculatory tissue beds *in vivo*.

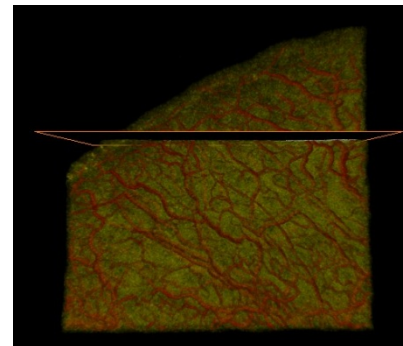
B-scan structure



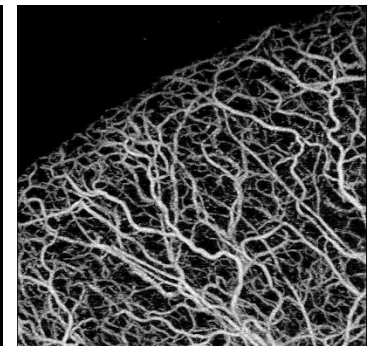
OMAG Cross-section



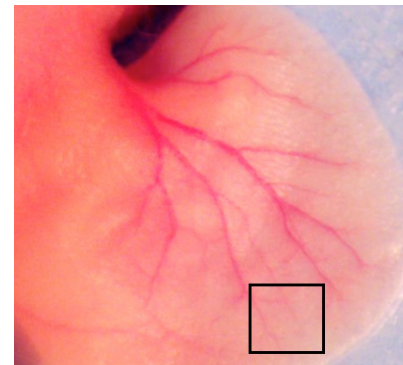
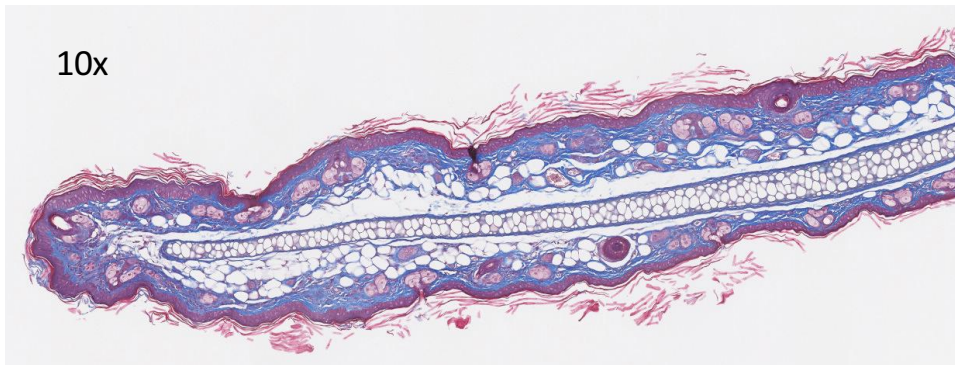
Volumetric OMAG (Red)
+ Structure (Yellow)



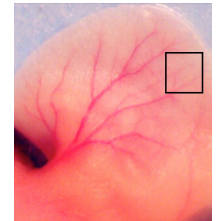
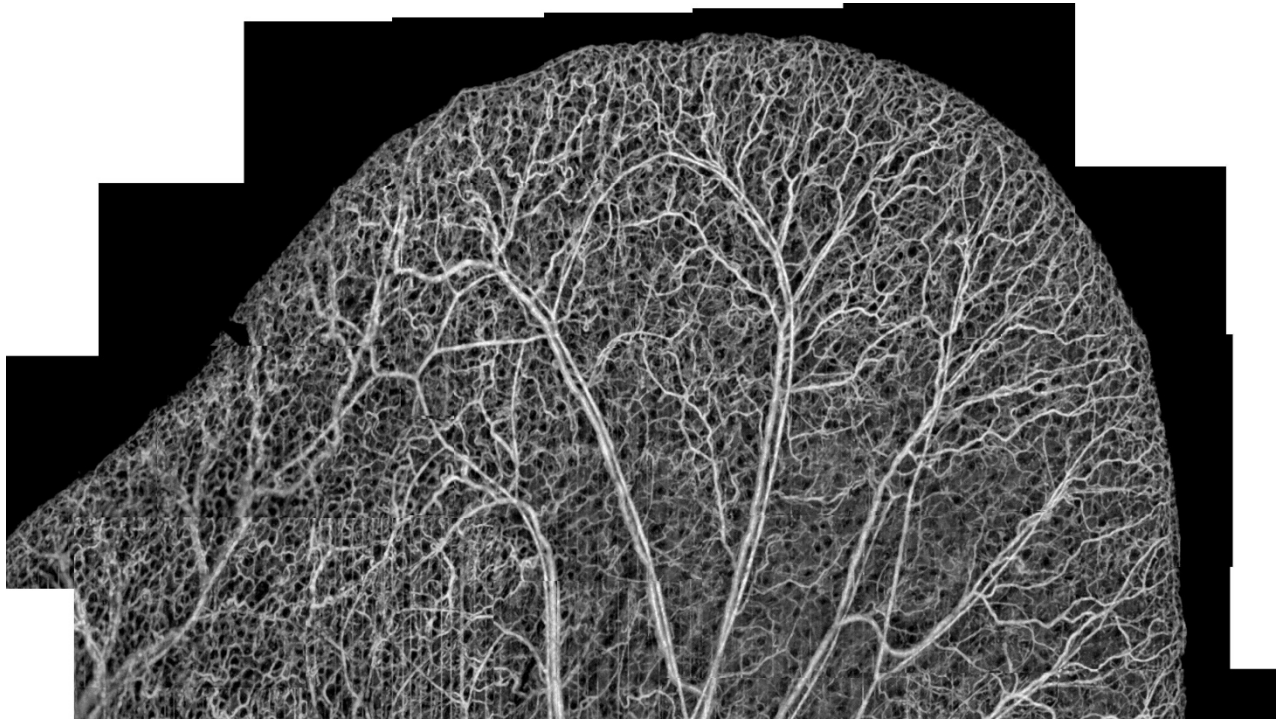
MIP blood vessels



10x



Large FOV mouse pinna microangiography



Eigendecomposition-based clutter filtering technique for optical micro-angiography

- Received A-line is modeled as superposition of three **independent** components: clutter (stationary tissue), red blood cells and noise.
- $X = [X_1, X_2, \dots, X_N]^T = c + b + n \quad \leftrightarrow \quad R_X = R_c + R_b + \sigma_n^2 I$
- Estimating the clutter subspace by the first largest components:

$$\widehat{R}_c = \frac{1}{M} \sum_{i=1}^M \widehat{R}_x = \frac{1}{M} \sum_{i=1}^M X_i X_i^H = E \Lambda E^H$$

$E = [e_1, e_2, \dots, e_N]$ is the unitary matrix of eigenvectors

- Filtered data (moving red blood cells) given by $Y = (I - \sum_i e_i e_i^H) \cdot X$

Problem Description

- Development of label-free and non-invasive imaging and quantification techniques to study wound healing progress *in vivo*.
 - Tissue structures
 - Blood flow perfusion
 - Lymphatic vessels
- This combination can be utilized to study therapeutic strategies for wound diseases such as diabetic ulcers.

Motivation

- Lack of non-invasive and label-free tools to study wound healing models at capillary level

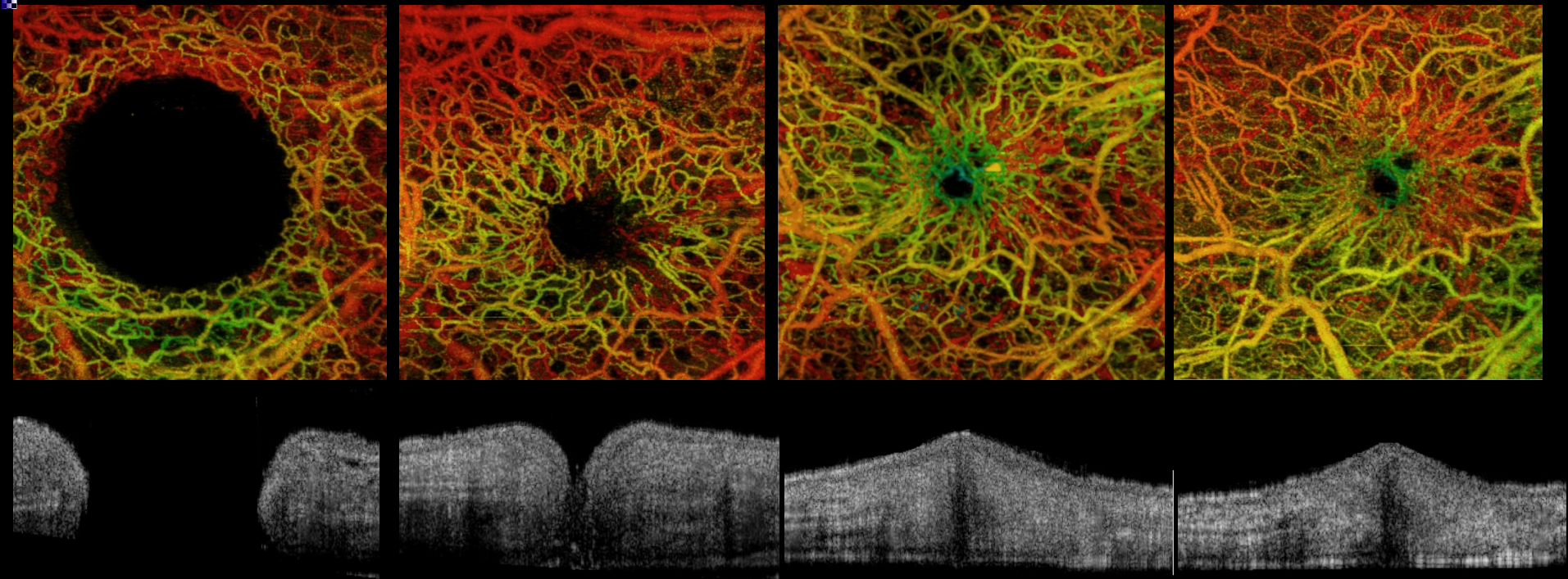
OCT Angiography for imaging wound healing

Week 1

Week 3

Week 5

Week 7



Translational Application

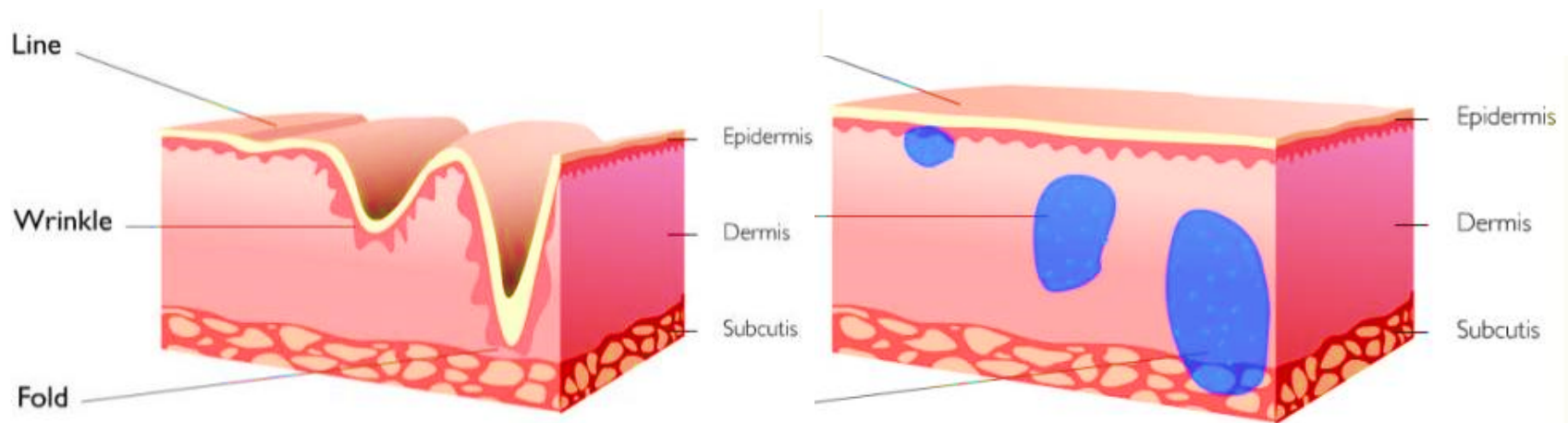
Complications of injectable dermal fillers



Injectable dermal fillers

- In the past decade, there has been a paradigm shift away from surgical procedures into minimally-invasive procedures

Invention of injectable dermal fillers to remove skin wrinkles





AMERICAN SOCIETY OF
PLASTIC SURGEONS®

2016 NATIONAL

Plastic Surgery Statistics

COSMETIC & RECONSTRUCTIVE PROCEDURE TRENDS

COSMETIC SURGICAL PROCEDURES	2016	2015	2000	2016 - VS - 2015	2016 - VS - 2000	COSMETIC MINIMALLY- INVASIVE PROCEDURES	2016	2015	2000	2016 - VS - 2015	2016 - VS - 2000
Breast augmentation (<i>Augmentation mammoplasty</i>)**	290,467	279,143	212,500	+4%	+37%	Botulinum Toxin Type A (<i>Botox®</i> , <i>Dysport®</i> , <i>Xeomin®</i>)***	7,056,255	6,757,198	786,911	+4%	+797%
Breast implant removals (<i>Augmentation patients only</i>)	28,467	24,661	40,787	+15%	-30%	Cellulite treatment (<i>Velosmooth®</i> , <i>Endermology</i>)	30,995	30,810	23,952	+1%	+29%
Breast lift (<i>Mastopexy</i>)	101,264	99,614	52,836	+2%	+92%	Chemical peel	1,360,850	1,310,252	1,149,457	+4%	+18%
Breast reduction (<i>Aesthetic patients only</i>)****	39,148	40,650	*	-4%	*	Injection lipolysis (<i>e.g.</i> , <i>Kybella®</i>)†	55,660	47,333	*	+18%	*
Breast reduction in men (<i>Gynecomastia</i>)	27,760	27,456	20,351	+1%	+36%	Intense Pulsed Light (IPL) treatment	656,781	646,592	*	+2%	*
Buttock augmentation with fat grafting****	18,489	14,705	*	+26%	*	Laser hair removal	1,109,385	1,116,708	735,996	-1%	+51%
Buttock implants****	2,999	2,540	*	+18%	*	Laser skin resurfacing	586,662	569,458	170,951	+3%	+243%
Buttock lift	4,251	4,767	1,356	-11%	+213%	Ablative	166,194	159,795	*	+4%	*
Calf augmentation****	419	514	*	-18%	*	Non-ablative (<i>Fraxel®</i> , <i>etc.</i>)	420,468	409,663	*	+3%	*
Cheek implant (<i>Malar augmentation</i>)	13,197	12,668	10,427	+4%	+27%	Laser treatment of leg veins	217,179	207,862	245,424	+4%	-12%
Chin augmentation (<i>Mentoplasty</i>)	16,688	17,451	26,924	-4%	-38%	Microdermabrasion	775,014	800,340	868,315	-3%	-11%
Dermabrasion	88,182	87,216	42,218	+1%	+109%	Non-invasive fat reduction (<i>e.g.</i> , <i>Coolsculpting®</i> , <i>Liposonix®</i>)†	333,082	318,144	*	+5%	*
Ear surgery (<i>Otoplasty</i>)	23,709	22,714	36,295	+4%	-35%	Non-surgical skin tightening (<i>e.g.</i> , <i>Pelleve®</i> , <i>Thermage®</i> , <i>Ulthera®</i>)†	306,089	291,821	*	+5%	*
Eyelid surgery (<i>Blepharoplasty</i>)	209,020	203,934	327,514	+2%	-36%	Sclerotherapy	323,009	322,280	866,555	0%	-63%
Facelift (<i>Rhytidectomy</i>)	131,106	125,711	133,856	+4%	-2%	Soft Tissue Fillers	2,600,868	2,550,987	652,885	+2%	+298%
Forehead lift	43,038	40,450	120,971	+6%	-64%	Acellular Dermal Matrix**** †	7,809	9,544	*	-18%	*
Hair transplantation	16,784	15,610	44,694	+8%	-62%	Calcium hydroxylapatite (<i>Radiesse®</i>)	242,563	256,256	*	-5%	*
Labiaplasty **** †	12,666	9,138	*	+39%	*	Collagen	14,126	14,353	587,615	-2%	-98%
Lip augmentation (<i>other than injectable materials</i>)	28,430	27,449	18,589	+4%	+53%	Porcine/bovine-based (<i>Evolence®</i> , <i>Zyderm®</i> , <i>Zyplast®</i>)	14,126	14,353	*	-2%	*
Lip reduction****	3,547	927	*	+283%	*	Fat	79,208	70,283	65,270	+13%	+21%
Liposuction	235,237	222,051	354,015	+6%	-34%	Hyaluronic acid (<i>Juvederm Ultra®</i> , <i>Juvederm Ultra Plus®</i> , <i>Perlane®</i> , <i>Restylane®</i> , <i>Belotero®</i>)	2,012,672	1,951,692	*	+3%	*
Lower body lift	11,299	8,431	207	+34%	+5358%	Platelet-Rich Plasma (PRP)†	102,101	100,719	*	+1%	*
Neck lift	55,227	54,281	*	+2%	*	Polyactic acid (<i>Sculptra®</i>)	125,044	130,089	*	-4%	*
Nose reshaping (<i>Rhinoplasty</i>)	223,018	217,979	389,155	+2%	-43%	Polymethyl-methacrylate microspheres (<i>Artefill®</i>)	17,345	18,051	*	-4%	*
Pectoral implants****	1,153	926	*	+25%	*	TOTAL / COSMETIC MINIMALLY-INVASIVE PROCEDURES ^^^^	15,411,829	14,969,785	5,500,446	+3%	+180%
Thigh Lift	9,929	9,192	5,303	+8%	+87%	TOTAL / COSMETIC PROCEDURES ^^^^	17,192,816	16,685,029	7,401,495	+3%	+132%
Tummy tuck (<i>Abdominoplasty</i>)	127,633	127,967	62,713	0%	+104%						
Upper arm lift	17,860	17,099	338	+4%	+5184%						

* Top 5 procedures

* Top 5 procedures

Variety of filler products in the cosmetic market

- **Permanent**

- Silicone
- Polymethylmethacrylate (PMMA) – acrylic glass or Plexiglas
- Polytetrafluoroethylene (PTFE) – Teflon

- **Semi-permanent**

- Collagen (Evolve)
- Calcium hydroxylapatite (Radiesse) - particle size 25-45 μm
- Poly-L-lactic acid (Sculptra) – particle size 40-63 μm

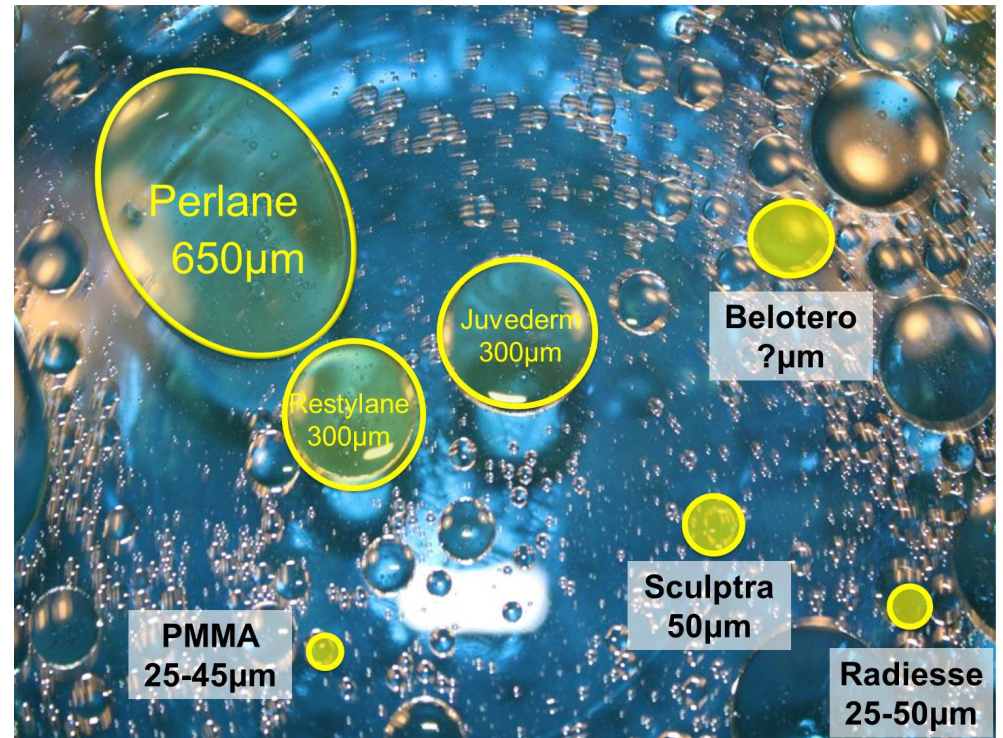
- **Dissolvable**

- Crosslinked hyaluronic acid
 - Restylane – particle size 300 μm
 - Juvederm – particle size 300 μm
 - Perlane – particle size 650 μm



Variety of dissolvable filler products

- Restylane (300 μm)
- Juvederm (300 μm)
- Perlane (650 μm)
- Belotero (variable)
- Radiesse (25 μm)



BELOTERO[®]



Perlane[®]

RADIESSE[®]
The magic ingredient is you™

Restylane[®]
Natural beauty from within



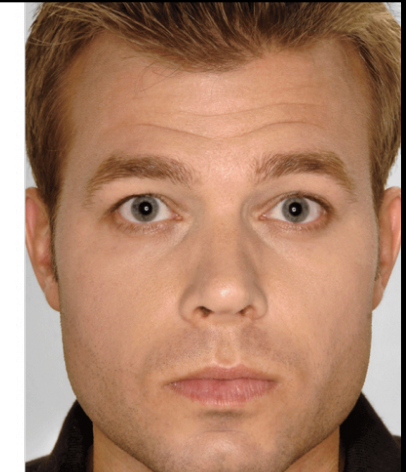
Before and after



Before

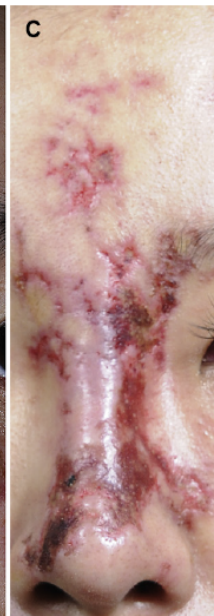
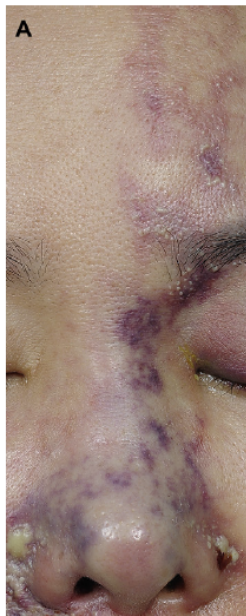


After

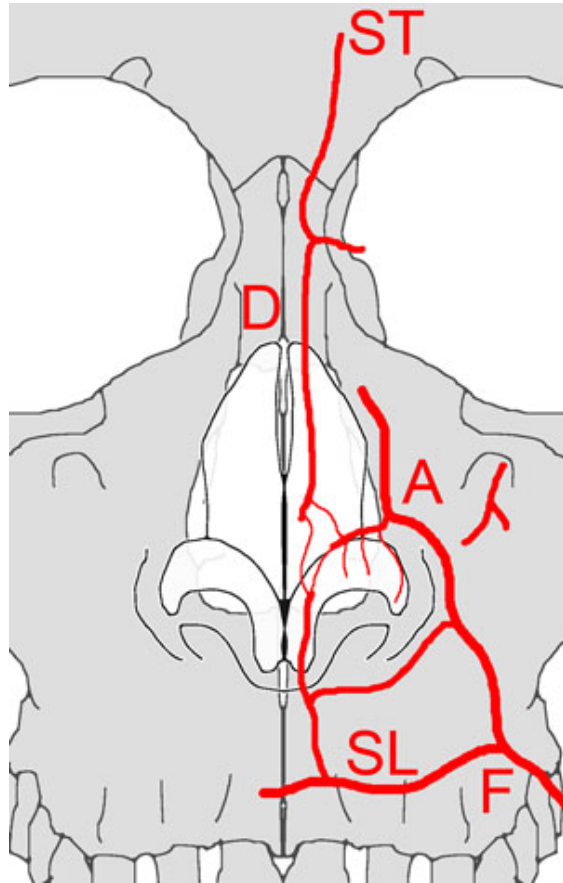


Complications!

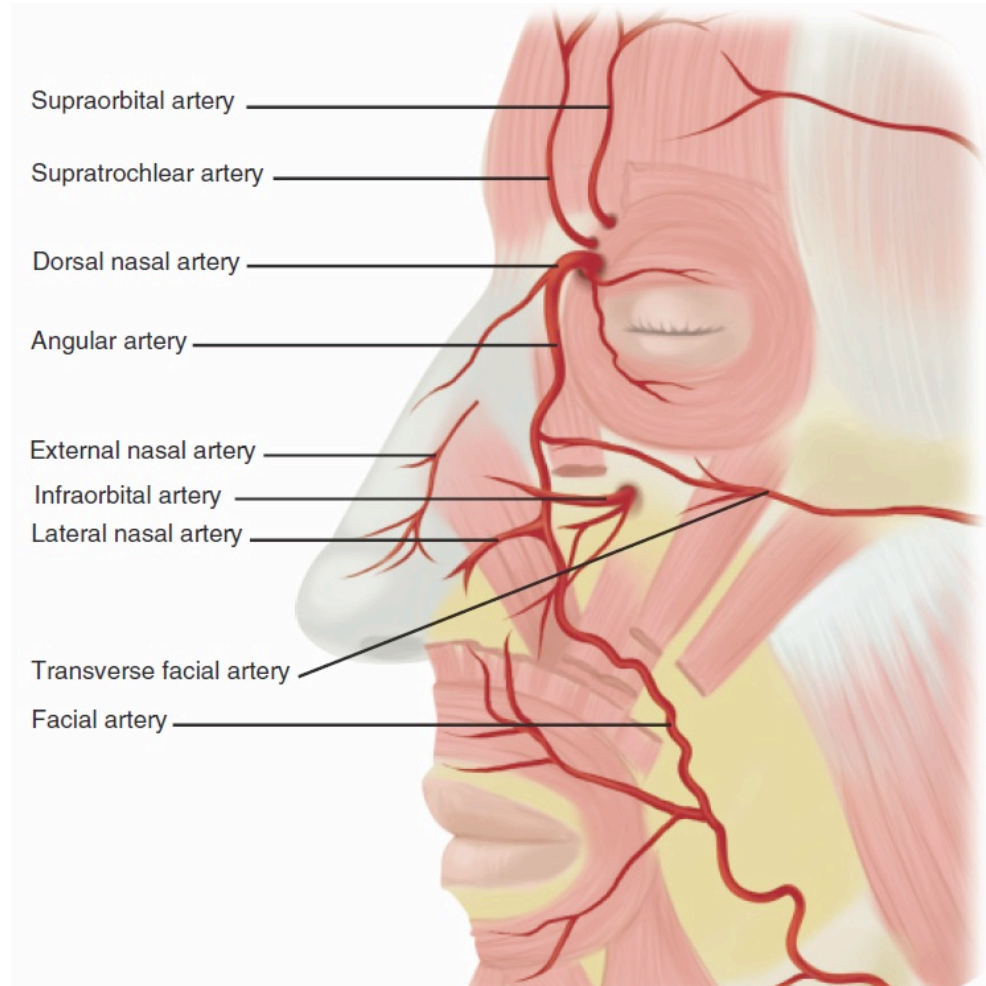
- Temporary: Bruising and erythema
- Permanent: Localized tissue necrosis
- Case reports: 9 in 10k



Nasal vasculature



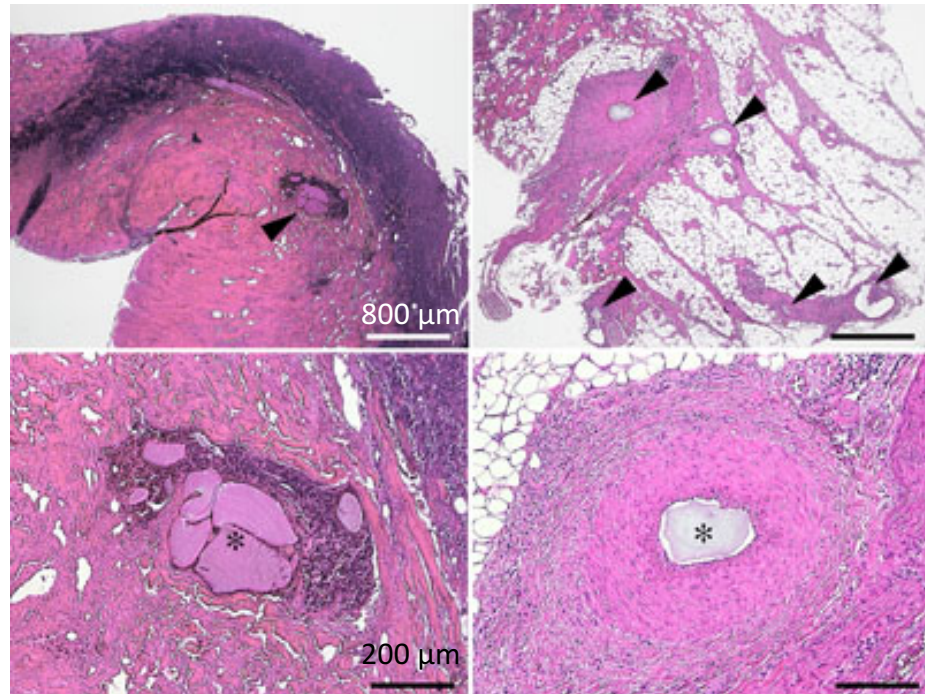
Loukas Surg Radiol Anat 2006



GRUNEBAUM et al., Dermatol Surg 2009

Histology of debridement sample

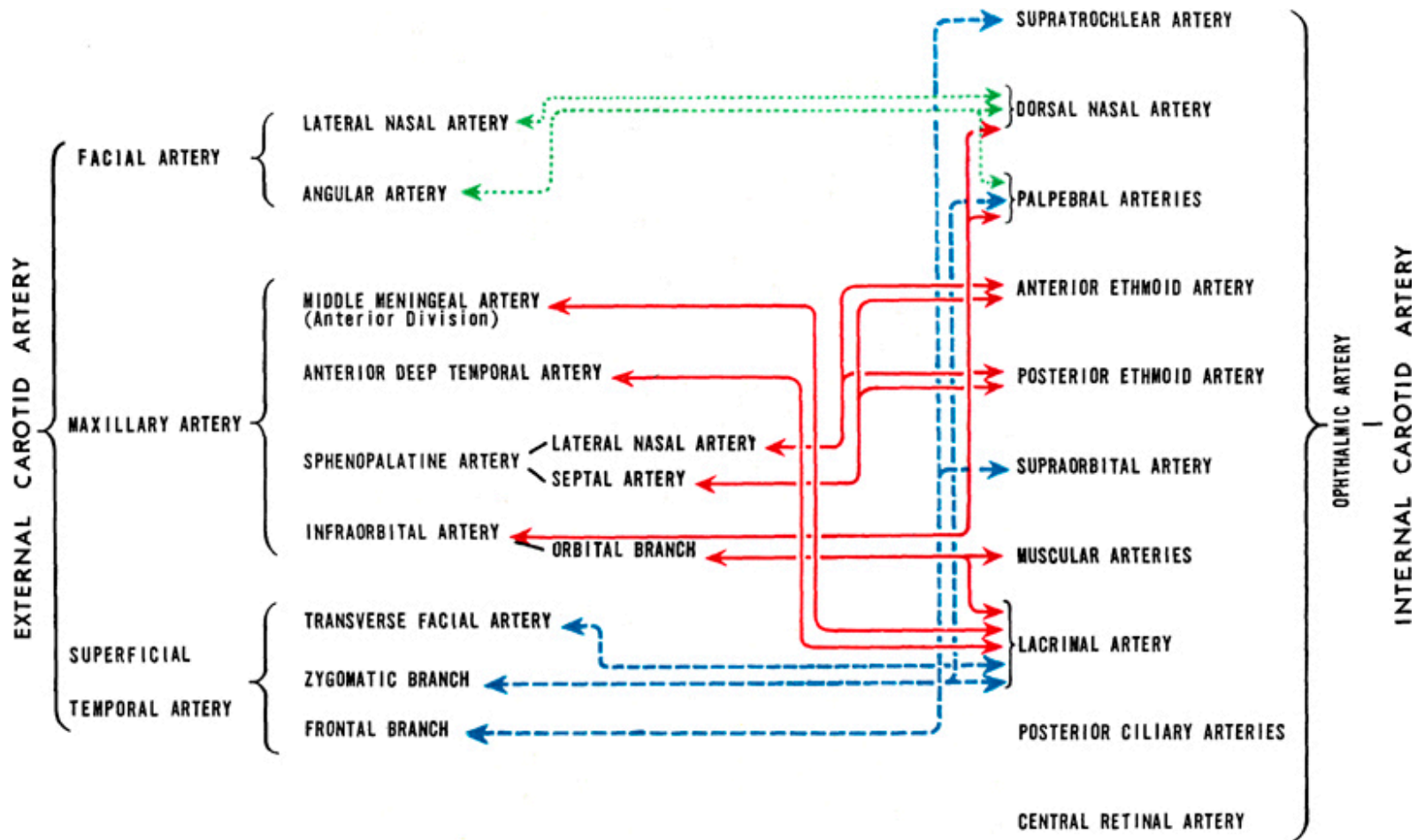
- Necrotic skin on the nasolabial fold
- Epidermal necrosis and intradermal deposition of filler material (arrow).
- Intra-arterial foreign bodies and thickening of the intima.
- Subcutaneous tissue shows multiple intra-arterial embolization (arrow)



Blindness! Central retinal artery occlusion

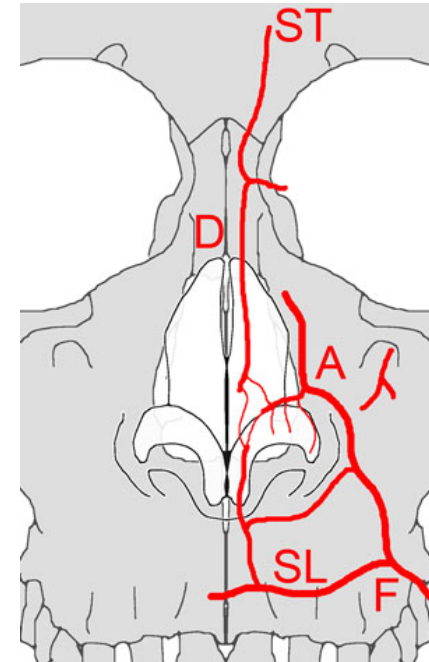
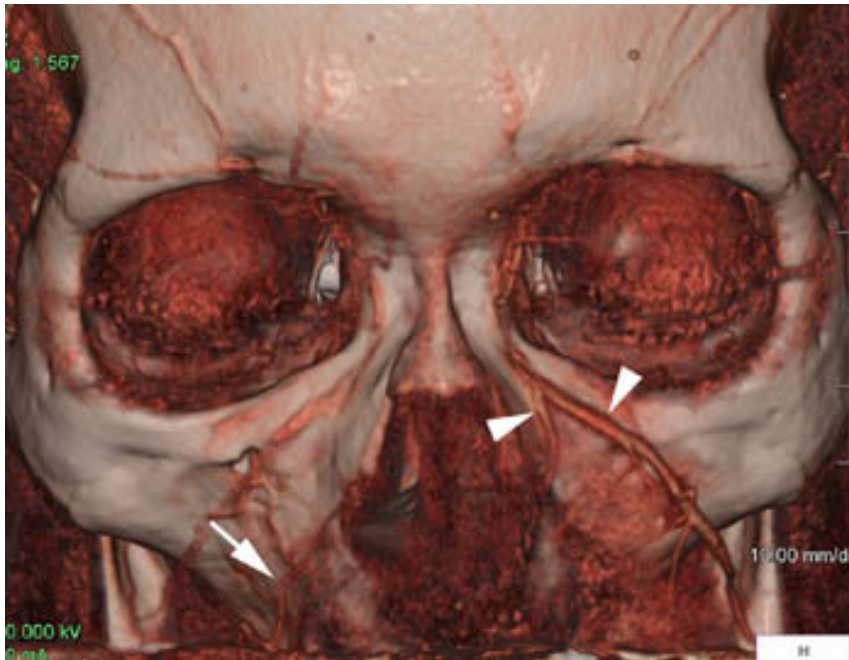


Anastomosis paths between internal and external carotid arteries through the face



3D computed tomographic angiography (3D-CTA)

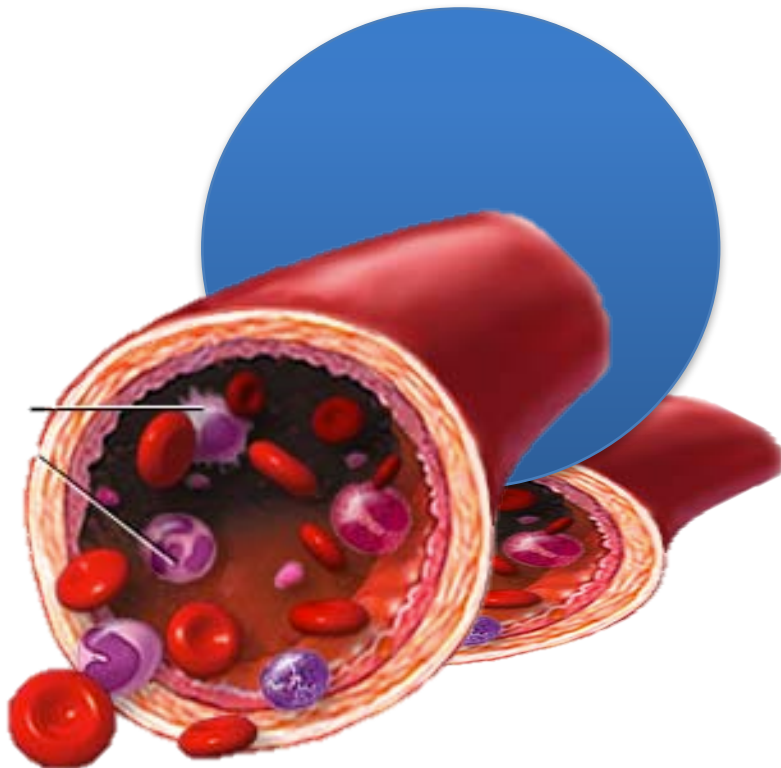
- Local occlusion of the left angular branch of the facial artery.



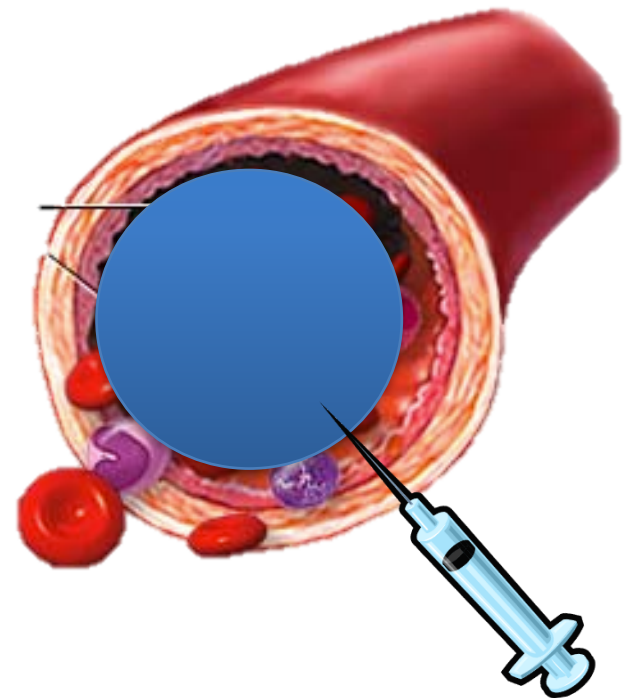
- Compensatory dilation of collateral vessels from the infraorbital artery was noted (arrowhead).

Proposed mechanisms

1-External vascular compression



2-Intravascular Occlusion



Our contribution

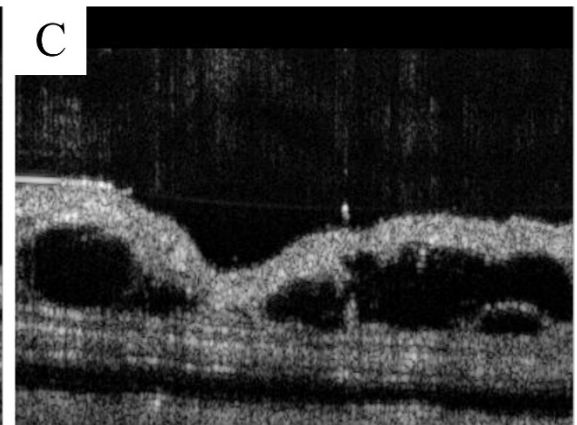
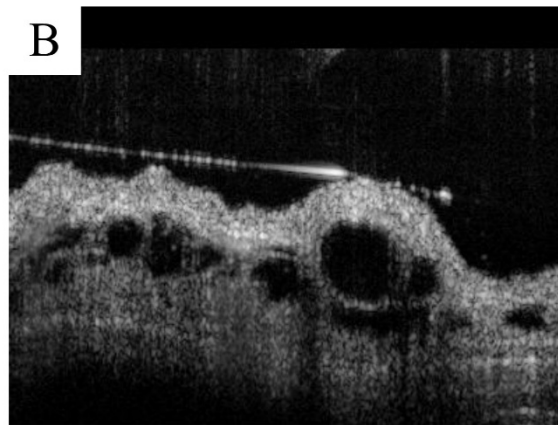
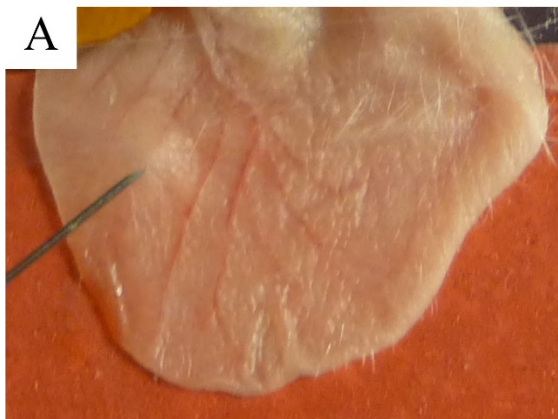
- Utilizing OCT angiography technology and an animal model to study complications associated with dermal filler injections
- Testing two hypothesis associated with these complications
- Pre-clinical studies

Motivation

- Understanding these mechanisms can help the clinicians to tailor therapeutic strategies after these incidents
- Towards development of better cosmetic filler materials to prevent microvascular complications

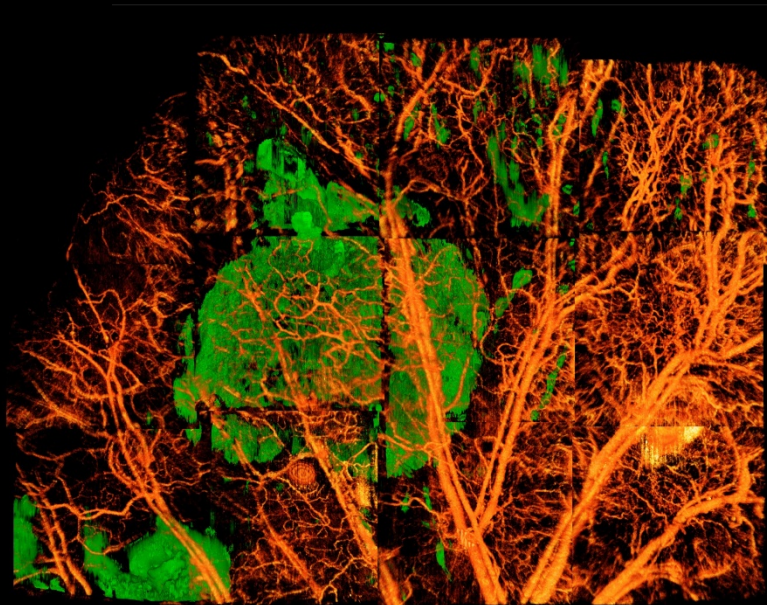
1- Testing extravascular compression theory

- Direct injection of various filler types into the mouse ear pinna
- Observe changes in the microcirculatory network around the filler
- Baseline image before injection, immediate after injection and 1-week follow up

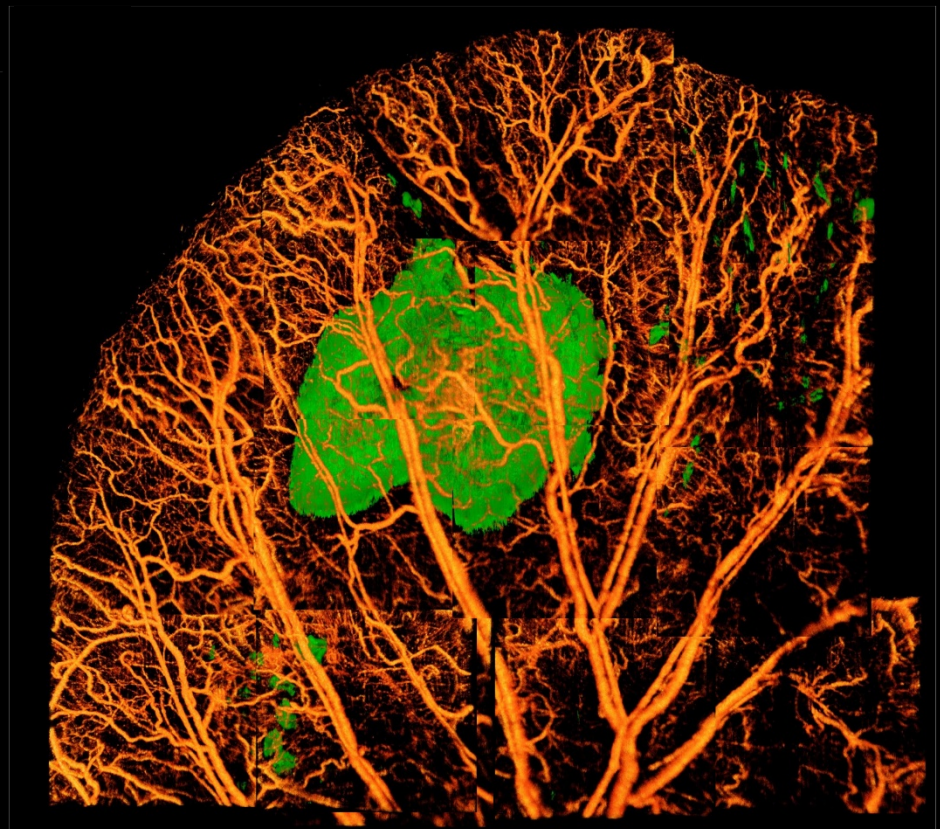


Soft tissue injection (Juvederm[®])

Immediate



Follow up

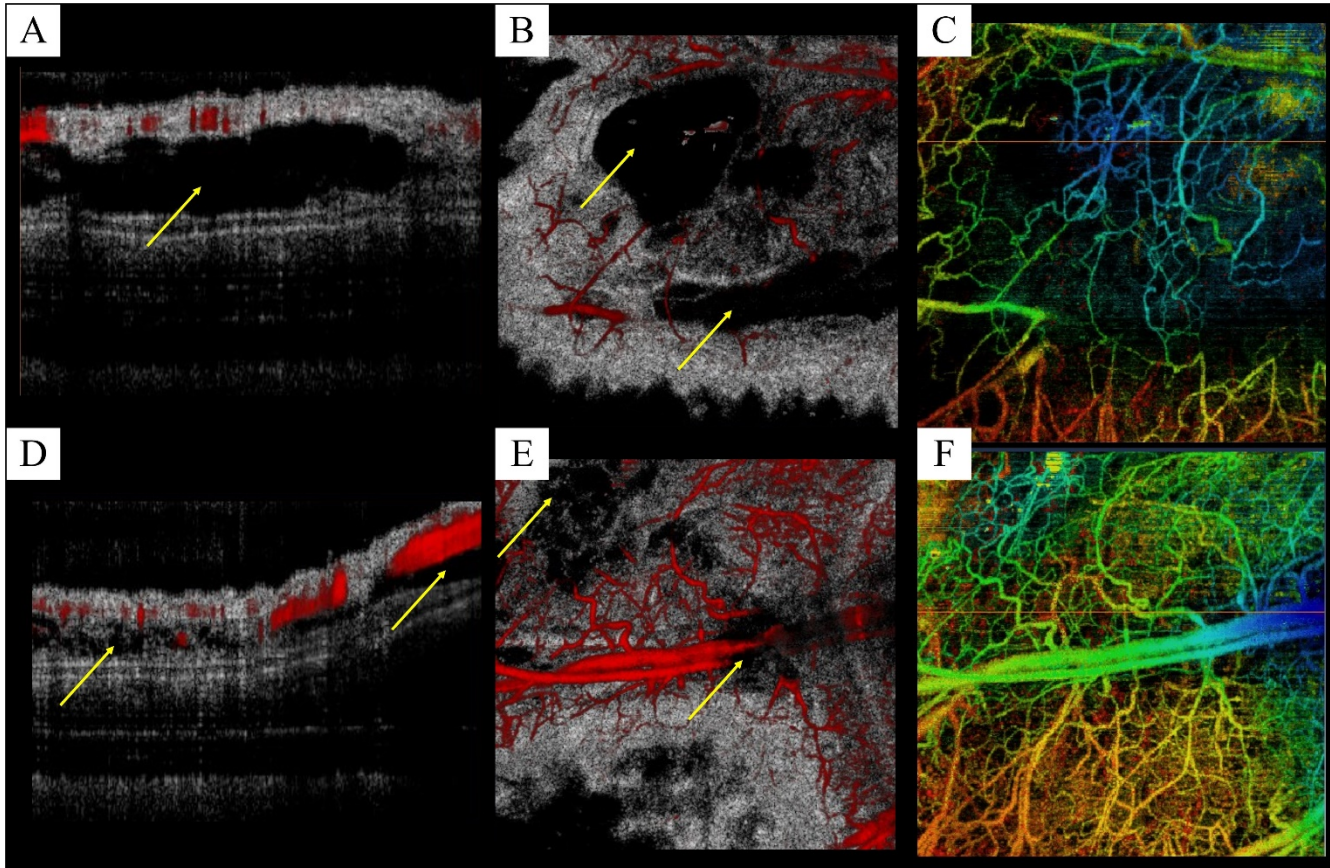


Soft tissue injection (Belotero[®])

Structure cross-sections overlaid with surrounding microvessels

Depth-encoded microvessels

Immediate



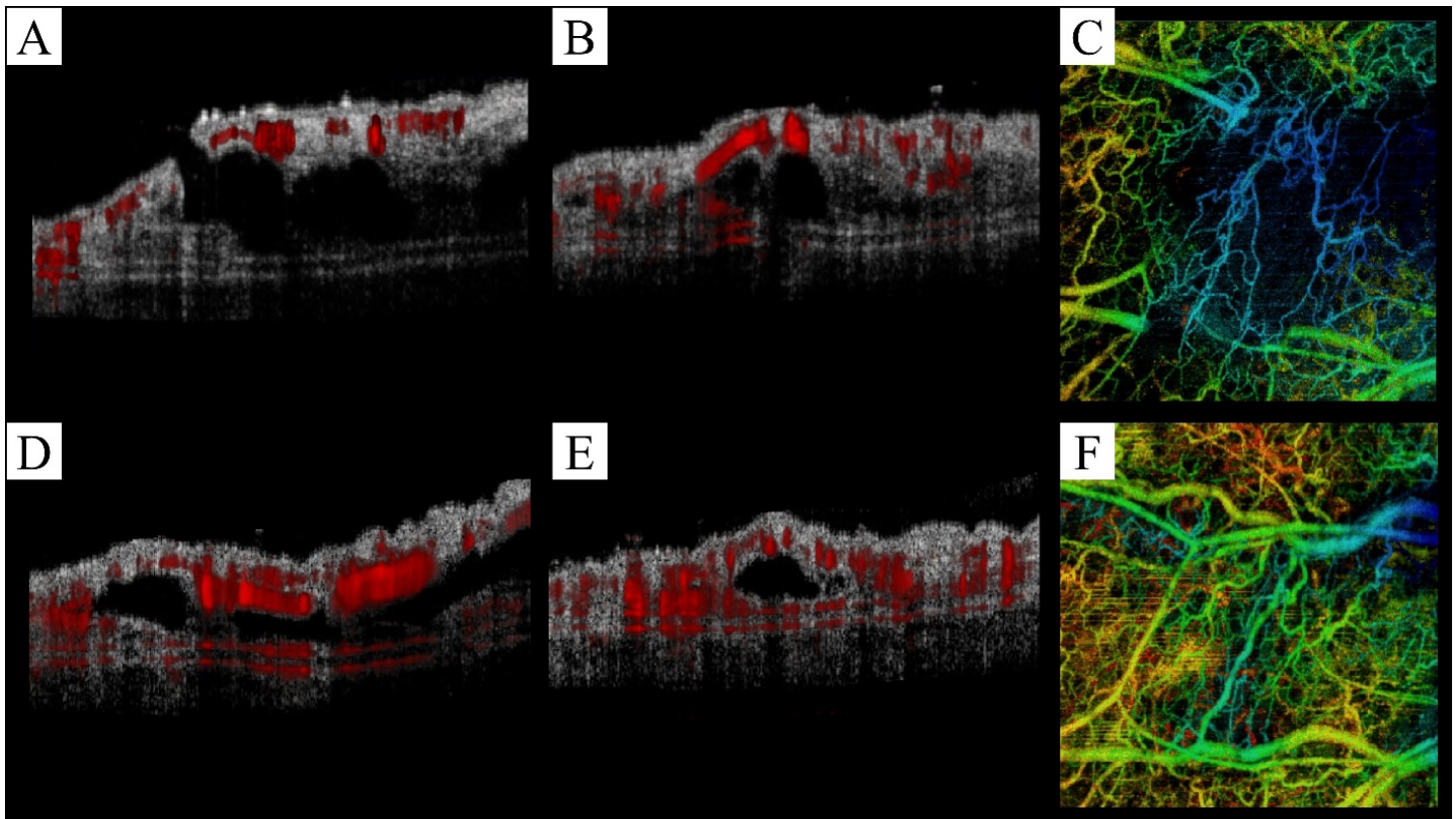
Follow up

Soft tissue injection (Restylane[®])

Structure cross-sections overlaid with surrounding microvessels

Depth-encoded microvessels

Immediate



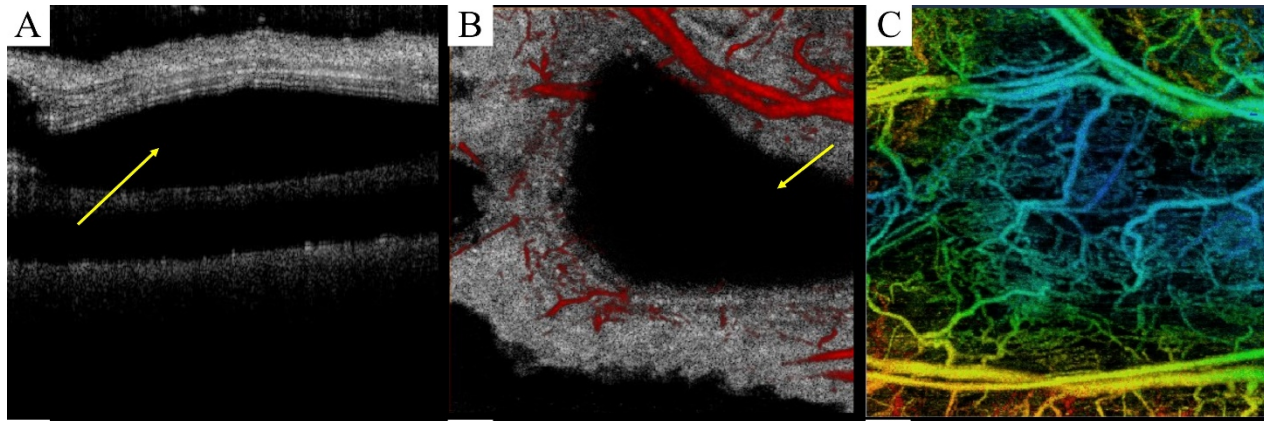
Follow up

Soft tissue injection (Voluma[®])

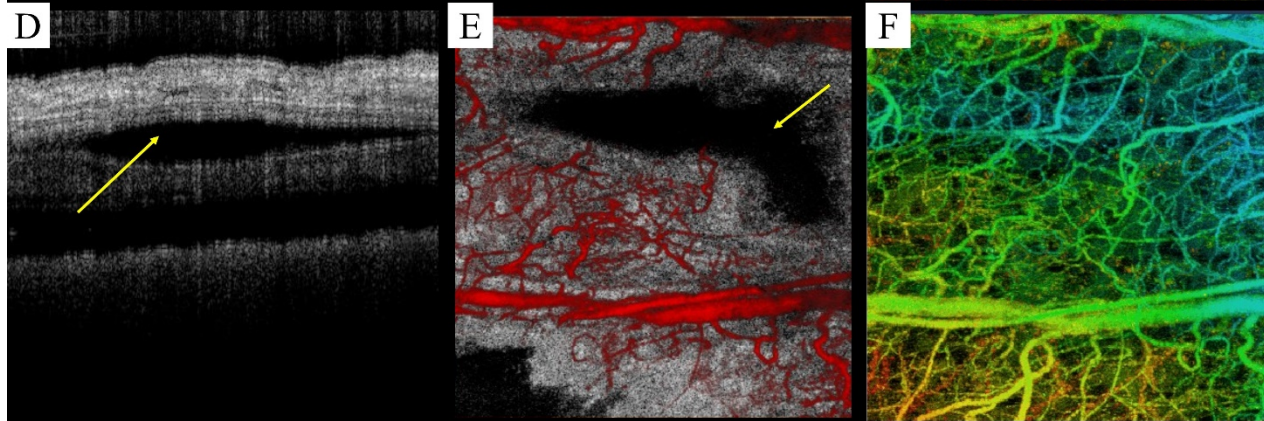
Structure cross-sections overlaid with surrounding microvessels

Depth-encoded microvessels

Immediate

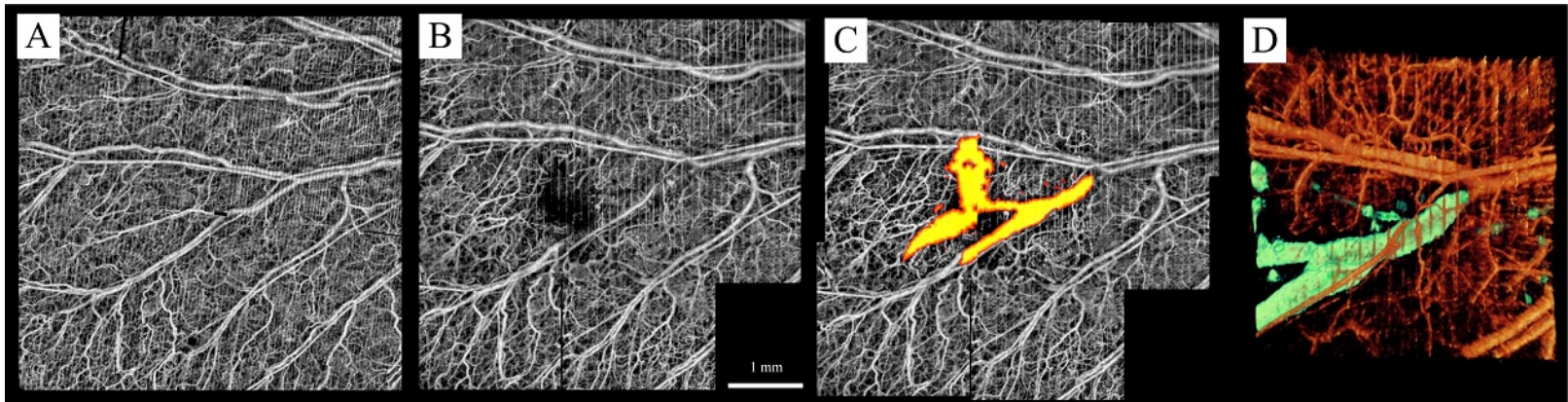


Follow up

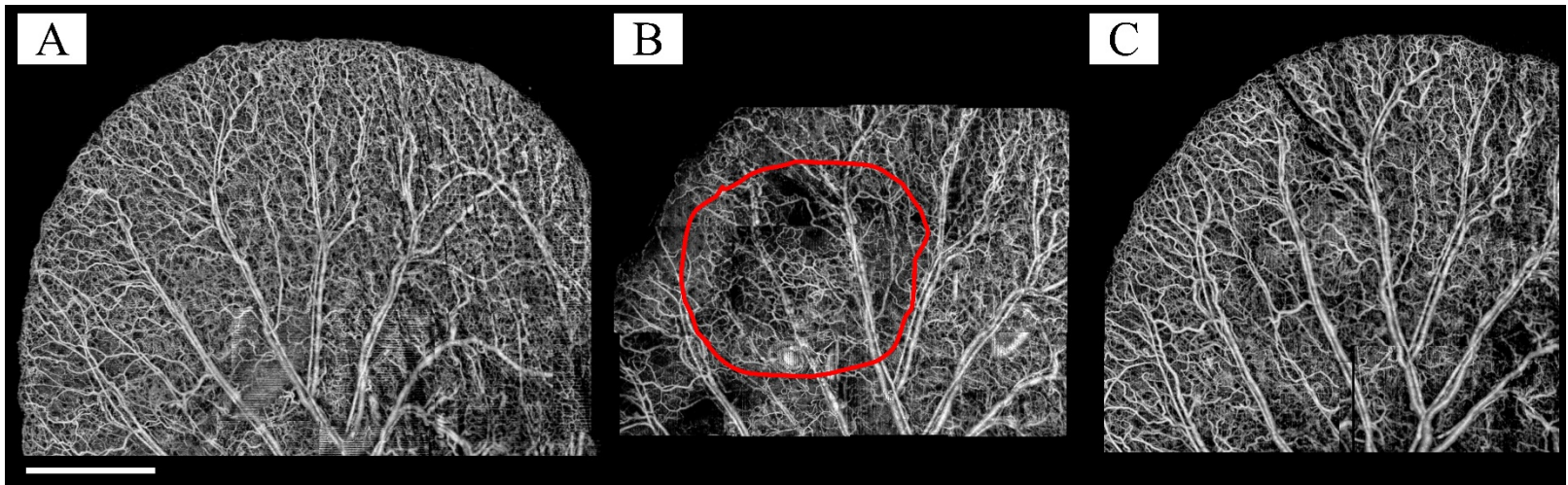


Possible damage to major veins? (Perlane®)

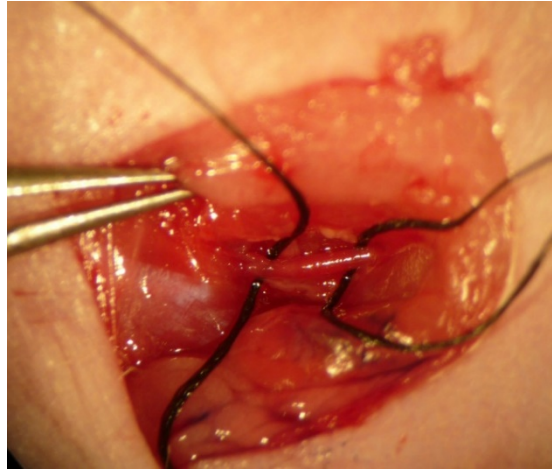
Case#1



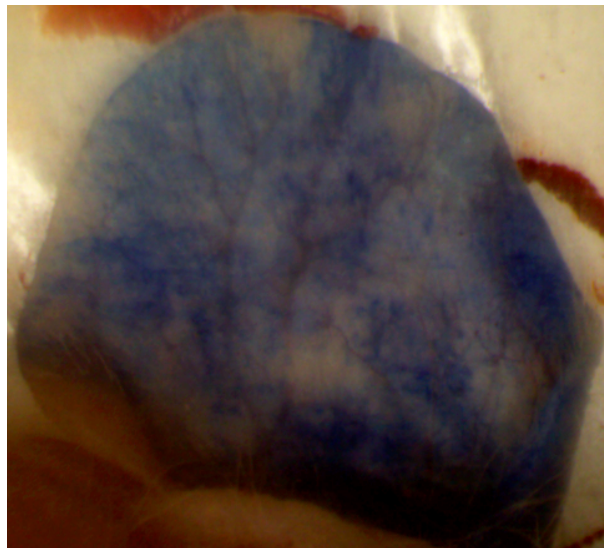
Case#2



2- Intravascular occlusion



Direct injection of diluted filler into the external carotid artery branch



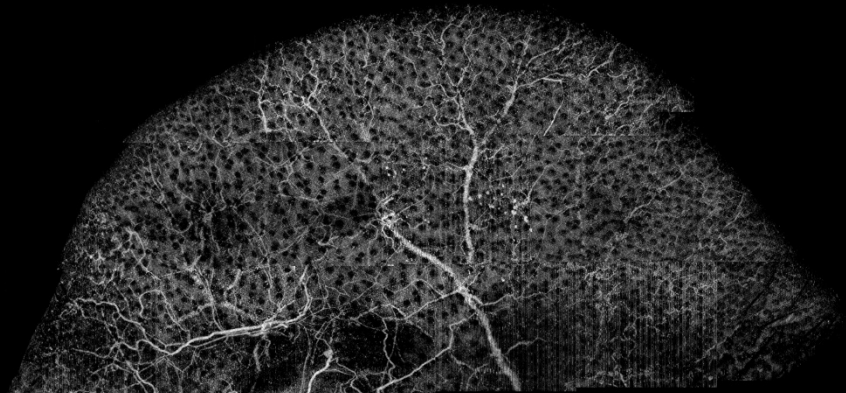
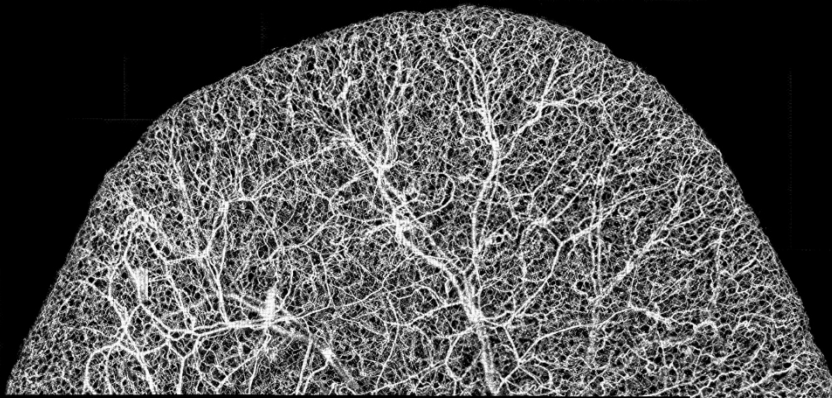
Evans Blue dye

Intravascular injection: Restylane and Voluma

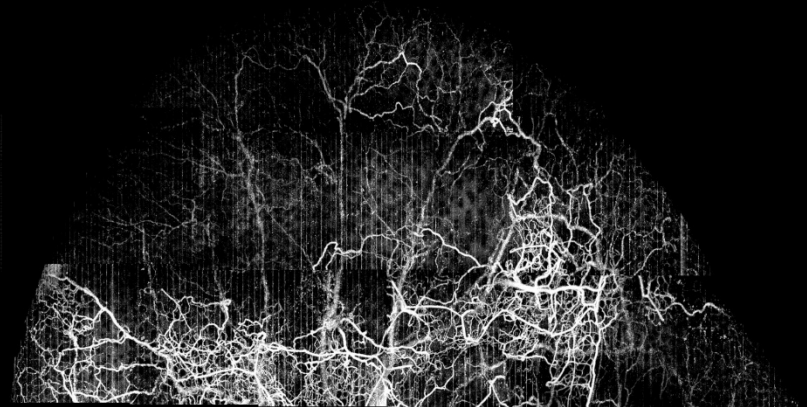
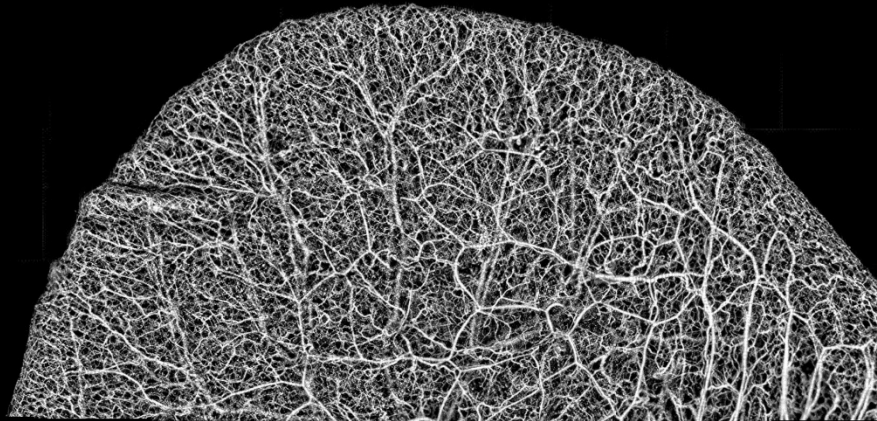
Baseline

Injection

Restylane



Voluma

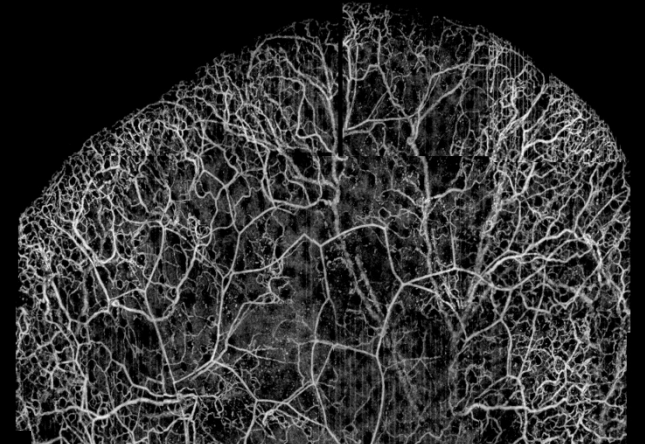
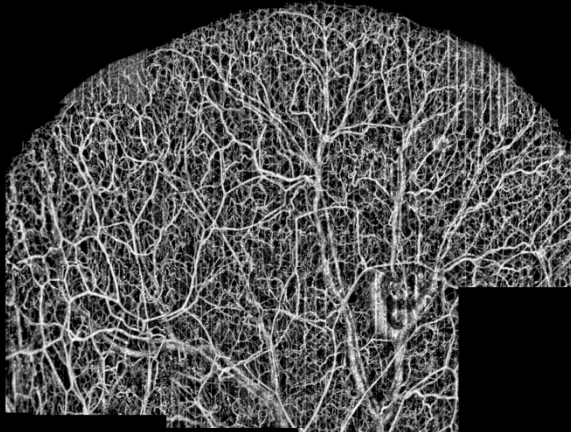


Intravascular injection: Juvederm and Belotero

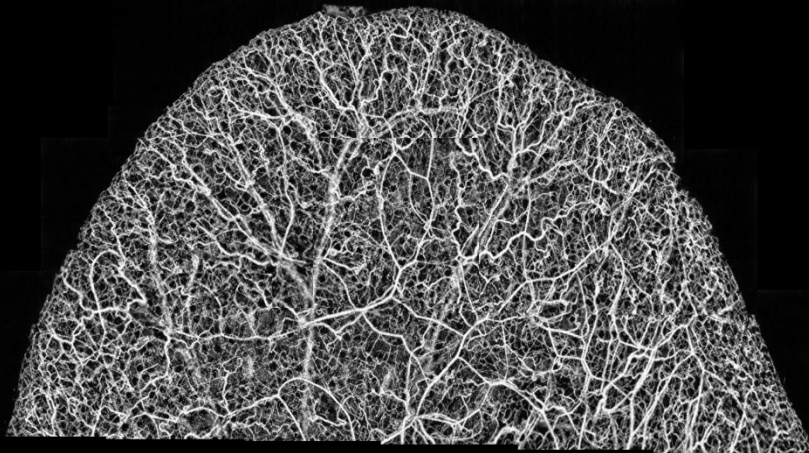
Baseline

Injection

Juvederm



Belotero



Conclusions

- Utilized OCT angiography techniques to study complications of cosmetic dermal fillers
- Tested two hypotheses: extravascular compression and intravascular occlusions
- Could not observe any major tissue necrosis and microvasculature blockage in extravascular compression experiment in the mouse ear model
- Fillers definitely blocked arteries when directly injected intravascular
- Histology validation in the future

Acknowledgments

UW Medicine
DEPARTMENT OF
OPHTHALMOLOGY

