ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ-ΙΑΤΡΙΚΗ ΣΧΟΛΗ
ΕΡΓΑΣΤΗΡΙΟ ΑΝΑΤΟΜΙΑΣ - "ΑΝΑΤΟΜΕΙΟ"
ΔΙΕΥΘΥΝΤΗΣ : ΚΑΘΗΓΗΤΗΣ ΘΕΟΔΩΡΟΣ Γ. ΤΡΟΥΠΗΣ

Η ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΑΓΓΕΙΑΚΗΣ ΑΝΑΤΟΜΙΑΣ ΤΟΥ ΚΡΟΤΑΦΙΚΟΥ ΒΟΘΡΟΥ
VASCULAR ANATOMY OF THE TEMPORAL FOSSA

ΑΝΔΡΕΑΣ ΝΙΚΟΛΗΣ, MD, MSc, FRCSC
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ΔΙΔΑΚΤΟΡΙΚΗ ΔΙΑΤΡΙΒΗ - PhD Thesis

ΑΘΗΝΑ 2021

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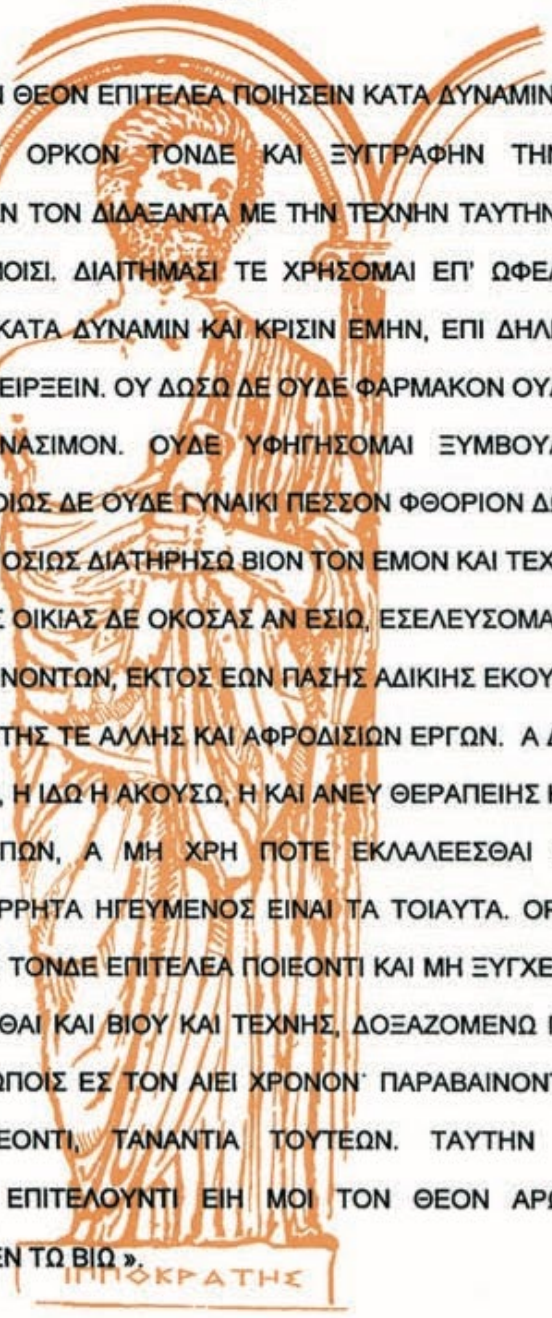
ΚΕΙΜΕΝΟ

« ΟΜΝΥΜΙ ΤΟΝ ΘΕΟΝ ΕΠΙΤΕΛΕΑ ΠΟΙΗΣΕΙΝ ΚΑΤΑ ΔΥΝΑΜΙΝ ΚΑΙ ΚΡΙΣΙΝ ΕΜΗΝ ΟΡΚΟΝ ΤΟΝΔΕ ΚΑΙ ΞΥΓΓΡΑΦΗΝ ΤΗΝΔΕ. ΗΓΗΣΕΣΘΑΙ ΜΕΝ ΤΟΝ ΔΙΔΑΞΑΝΤΑ ΜΕ ΤΗΝ ΤΕΧΝΗΝ ΤΑΥΤΗΝ ΙΣΑ ΓΕΝΕΤΗΣΙΝ ΕΜΟΙΣΙ. ΔΙΑΙΤΗΜΑΣΙ ΤΕ ΧΡΗΣΟΜΑΙ ΕΠ' ΩΦΕΛΕΙΗ ΚΑΜΝΟΝΤΩΝ ΚΑΤΑ ΔΥΝΑΜΙΝ ΚΑΙ ΚΡΙΣΙΝ ΕΜΗΝ, ΕΠΙ ΔΗΛΗΣΕΙ ΔΕ ΚΑΙ ΑΔΙΚΙΗ ΕΙΡΞΕΙΝ. ΟΥ ΔΩΣΩ ΔΕ ΟΥΔΕ ΦΑΡΜΑΚΟΝ ΟΥΔΕΝΙ ΑΙΤΗΘΕΙΣ ΘΑΝΑΣΙΜΟΝ. ΟΥΔΕ ΥΦΗΓΗΣΟΜΑΙ ΞΥΜΒΟΥΛΙΗΝ ΤΟΙΗΝΔΕ. ΟΜΟΙΩΣ ΔΕ ΟΥΔΕ ΓΥΝΑΙΚΙ ΠΕΣΣΟΝ ΦΘΟΡΙΟΝ ΔΩΣΩ. ΑΓΝΩΣ ΔΕ ΚΑΙ ΟΣΙΩΣ ΔΙΑΤΗΡΗΣΩ ΒΙΟΝ ΤΟΝ ΕΜΟΝ ΚΑΙ ΤΕΧΝΗΝ ΤΗΝ ΕΜΗΝ. ΕΣ ΟΙΚΙΑΣ ΔΕ ΟΚΟΣΑΣ ΑΝ ΕΣΙΩ, ΕΣΕΛΕΥΣΟΜΑΙ ΕΠ' ΩΦΕΛΕΙΗ ΚΑΜΝΟΝΤΩΝ, ΕΚΤΟΣ ΕΩΝ ΠΑΣΗΣ ΑΔΙΚΙΗΣ ΕΚΟΥΣΙΗΣ ΚΑΙ ΦΘΟΡΙΗΣ ΤΗΣ ΤΕ ΑΛΛΗΣ ΚΑΙ ΑΦΡΟΔΙΣΙΩΝ ΕΡΓΩΝ. Α Δ' ΑΝ ΕΝ ΘΕΡΑΠΕΙΗ, Η ΙΔΩ Η ΑΚΟΥΣΩ, Η ΚΑΙ ΑΝΕΥ ΘΕΡΑΠΕΙΗΣ ΚΑΤΑ ΒΙΟΝ ΑΝΘΡΩΠΩΝ, Α ΜΗ ΧΡΗ ΠΟΤΕ ΕΚΛΑΛΕΕΣΘΑΙ ΕΞΩ, ΣΙΓΗΣΟΜΑΙ, ΑΡΡΗΤΑ ΗΓΕΥΜΕΝΟΣ ΕΙΝΑΙ ΤΑ ΤΟΙΑΥΤΑ. ΟΡΚΟΝ ΜΕΝ ΟΥΝ ΜΟΙ ΤΟΝΔΕ ΕΠΙΤΕΛΕΑ ΠΟΙΕΟΝΤΙ ΚΑΙ ΜΗ ΞΥΓΧΕΟΝΤΙ ΕΙΗ ΕΠΑΥΡΑΣΘΑΙ ΚΑΙ ΒΙΟΥ ΚΑΙ ΤΕΧΝΗΣ, ΔΟΞΑΖΟΜΕΝΩ ΠΑΡΑ ΠΑΣΙΝ ΑΝΘΡΩΠΟΙΣ ΕΣ ΤΟΝ ΑΙΕΙ ΧΡΟΝΟΝ· ΠΑΡΑΒΑΙΝΟΝΤΙ ΔΕ ΚΑΙ ΕΠΙΟΡΚΕΟΝΤΙ, ΤΑΝΑΝΤΙΑ ΤΟΥΤΕΩΝ. ΤΑΥΤΗΝ ΤΗΝ ΕΠΑΓΓΕΛΙΑΝ ΕΠΙΤΕΛΟΥΝΤΙ ΕΙΗ ΜΟΙ ΤΟΝ ΘΕΟΝ ΑΡΩΓΟΝ ΚΤΗΣΑΣΘΑΙ ΕΝ ΤΩ ΒΙΩ ».



Curriculum Vitae

Dr. Andreas Nikolis MD, MSc, FRCSC

I. PERSONAL INFORMATION

- Date of birth: September 26, 1969
- Languages (spoken and written): English, French, Greek
- E-mail: an@nikolis.net
- Office address: 376 Victoria Suite 400, Westmount, Quebec, Canada H3Z1C3.

II. CURRENT POSITIONS

- Associate Professor of Surgery, Department of Plastic and Reconstructive Surgery, McGill University, Sept 2019- current
- Associate Professor of Surgery, Department of Plastic and Reconstructive Surgery, Université de Montréal, Sept 2010- current
- Medical Director, Westmount Aesthetic Surgery Centre, 245 Victoria, Suite 300 Westmount QC (2015- current)
- National Medical Director, Victoria Park Medispas, Westmount, West Island, Downtown Montreal, Laval, Gatineau, Ottawa, Quebec City (2008- current)

PAST POSITIONS:

- Director for Aesthetic Surgery Residency Program, Université de Montréal (July 2015- July 2017)
- Scientific Collaborator, Department of Physiology, University of Athens, Athens Greece. (2011-2018)
- Director, Victoria Park Research Center, 376 Victoria, Westmount QC (January 2011- current)
- Director of Research, Division of Plastic Surgery, Université de Montréal (July 2009-July 2010)
- Director of Research, Plastic Surgery, Centre Hospitalier de l'Université de Montréal (July 2005-June 2009)
- Director of Research, Programme Universitaire de Reimplantation Provinciale (Quebec Provincial Replantation Program) (Sept 2004- Sept 2010)
- Assistant Professor of Surgery, Department of Plastic and Reconstructive Surgery, Université de Montréal (2004-10)
- Acting Chief, Chef Adjointe, Chirurgie Plastique, CHUM (July 2005-July 2010)
- Wound healing committee: Centre Hospitalier de l'Université de Montréal (Sept 2006-Sept 2009)
- Admissions Committee, Plastic Surgery Residency program (2006-2009, 2012, 2013, 2014) (Academic Year July 1-June 30)
- Program Committee, Plastic Surgery Residency program (2006-2009, 2012, 2013, 2014) (Academic Year July 1-June 30)

III. EDUCATION

Center	Department	Degree-Title	Year
National and Kapodistrian University of Athens	Medicine	PhD	2018 - 2021
Institute for Craniofacial & Reconstructive Surgery Dr. Ian T Jackson	Craniofacial Surgery	Fellowship	2002 - 2003
McGill University	Experimental Surgery	MSc	2000 - 2002
University of Montreal	Plastic Surgery	Residency	2000 - 2002
McGill University	General Surgery	Residency	1996 - 2000
Queen's University	Medicine	MD	1992 - 1996
McGill University	Epidemiology	Graduate Studies	1991 - 1992
McGill University	Anatomy	BSc	1988 - 1991

IV. LICENCENSURE

- MD: CANADA (Quebec), Status: Active
- MD: EUROPE (Greece), Status: Active
- PLASTIC SURGERY: FRCSC, Status: Active
- PLASTIC SURGERY: Europe
(HELLENIC BOARD OF PLASTIC SURGERY) Status: Active

V. RESEARCH STUDENTS

MSc/PhD Thesis Director - Université de Montréal

- Miss Kaitlyn Enright – PhD Thesis: Prospective evaluation of adverse events in facial injectable aesthetics. (2017-21)
- Dr. Demetrios Rizis – Thesis: Breast Reconstruction registry tool development. (2012-13)
- Dr. Véronique St-Supéry - Thesis: Evaluation of a new animal model in tendon repair. (2008-2010)
- Dr. Genevieve Landes - Thesis: Evaluating the role of antibiotic prophylaxis in plastic surgery. (2009)
- Dr. Zahi Abou Chacra - Thesis: MGMT Methylation Prevalence in Head and Neck Squamous Cell Cancer (2010)

VI. PUBLICATIONS

* denotes medical student, resident, or graduate student

PUBLISHED 2021:

1. *Safran T, Swift A, Cotofana S, **Nikolis A**. Evaluating safety in hyaluronic acid lip injections. Expert Opin Drug Saf. 2021 Aug 19:1-14. doi: 10.1080/14740338.2021.1962283. Epub ahead of print. PMID: 34328377.

2. Cotofana S, Hamade H, Bertucci V, Fagien S, Green JB, Pavicic T, **Nikolis A**, Lachman N, Hadjab A, Frank K. Change in Rheologic Properties of Facial Soft-Tissue Fillers across the Physiologic Angular Frequency Spectrum. Plast Reconstr Surg. 2021 Aug 1;148(2):320-331. doi: 10.1097/PRS.0000000000008188. PMID: 34398083.

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3. **Nikolis A**, Berros P, Enright KM, Cordoba M, Nguyen Q. A Randomized, Crossover-Controlled Evaluator-Blinded Trial Evaluating Cannula- Vs Needle-Assisted Hyaluronic Acid Injections for Infraorbital Deformities. Aesthet Surg J. 2021 Jul 20:sjab284. doi: 10.1093/asj/sjab284. Epub ahead of print. PMID: 34282831.

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5. **Nikolis A**. Response to: Shockwave Therapy for the Prevention of Paradoxical Adipose Hyperplasia After Cryolipolysis: Myth or Reality? Aesthet Surg J. 2021 Jul 14;41(8):NP1139-NP1140. doi: 10.1093/asj/sjab176. PMID: 33884403.

6. Bertucci V, **Nikolis A**, Solish N, Lane V, Hicks J. Efficacy and Safety of Flexible Hyaluronic Acid Fillers in Lip and Perioral Enhancement. J Drugs Dermatol. 2021 Apr 1;20(4):402-408. doi: 10.36849/JDD.2021.5525. PMID: 33852235.

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8. **Nikolis A**, Frank K, Guryanov R, Gombolevskiy V, Morozov S, Makhmud K, Chernina V, Gotkin RH, Green JB, Cotofana S. Differences in Temporal Volume between Males and Females and the Influence of Age and BMI: A Cross-Sectional CT-Imaging Study. Facial Plast Surg. 2021 Mar 8. doi: 10.1055/s-0041-1725201. Epub ahead of print. PMID: 33684952.

9. Bertucci V, **Nikolis A**, Solish N, Lane V, Hicks J. Subject and partner satisfaction with lip and perioral enhancement using flexible hyaluronic acid fillers. J Cosmet Dermatol. 2021 May;20(5):1499-1504. doi: 10.1111/jocd.13956. Epub 2021 Feb 1. PMID: 33522714.

10. Nestor M, Cohen JL, Landau M, Hilton S, **Nikolis A**, Haq S, Viel M, Andriopoulos B, Prygova I, Foster K, Redaelli A, Picaut P. Onset and Duration of AbobotulinumtoxinA for Aesthetic Use in the Upper face: A Systematic Literature Review. J Clin Aesthet Dermatol. 2020 Dec;13(12):E56-E83. Epub 2020 Dec 1. PMID: 33488922; PMCID: PMC7819591.

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15. Rosengaus F, **Nikolis A**. Cannula versus needle in medical rhinoplasty: the nose knows. J Cosmet Dermatol. 2020 Dec;19(12):3222-3228. doi: 10.1111/jocd.13743. Epub 2020 Oct 11. PMID: 32991042.

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18. **Nikolis A**, Enright KM**.** Commentary: "Evaluating the role of small particle hyaluronic acid fillers using micro-droplet technique in the face, neck and hands: A retrospective chart review" J Dermatol & Skin Sci. 2020;2(1):26-28

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20. **Nikolis A**, Enright K, Lazarova D, Sampalis JS. The role of clinical examination in midface volume correction using hyaluronic acid fillers. Should patients be stratified by skin thickness? Aesthetic surgery open forum. *Aesthetic Surgery Journal Open Forum*, Volume 2, Issue 1, January 2020, ojaa005

21. Cotofana S, Alfertshofer M, Frank K, Bertucci V, Beleznay K, **Nikolis A**, Sykes J, Swift A, Lachman N, Schenck TL. Relationship Between Vertical Glabellar Lines and the Supratrochlear and Supraorbital Arteries. Aesthet Surg J. 2020 May 29:sjaa138. doi: 10.1093/asj/sjaa138

22. Cotofana S, Gaete A, Hernandez CA, Casabona G, Bay S, Pavicic T, Coimbra D, Suwanchinda A [8] Swift A, Green J, **Nikolis A**, Frank K. The Six Different Injection Techniques for the Temple – Clinical Anatomy and Danger Zones. J Cosmet Dermatol. 2020 May 17. doi: 10.1111/jocd.13491

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23. *Enright KM, **Nikolis A.** In vivo determination of the skin surface topography and biophysical properties of human hands: Effects of sex and hand dominance. Skin Res Technol. 2019 Oct 18.

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27. **Nikolis A**, Enright K, Sapra S, Khanna J. A Multicenter, Retrospective Evaluation of Tissue Stabilized-Guided Subcision in the Management of Cellulite. ACCEPTED: Aesthetic Surgery Journal, 2018

28. **Nikolis A**, Enright K. Methods of standardizing photography for cellulite in the buttock and the posterior thighs. Dermatol Surg. 2018 Sep 10. Epub ahead of print.

29. **Nikolis A,** Enright KM, Masouri S, Bernstein S, Antoniou C. Prospective evaluation of incobotulinumtoxinA in the management of the masseter using two different injection techniques. Clin Cosmet Investig Dermatol. 2018 Jul 12;11:347-356.

30. **Nikolis A.** Commentary on: A Single Center, Prospective, Randomized, Sham-Controlled, Double-Blinded, Split-Face Trial Using Microinjections of Transparent Hyaluronic Acid Gel for Cheek Rejuvenation. Dermatol Surg. 2018 Jan 29

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33. **Nikolis A**, Fauverghe S, Vezina D, Scapagnini G. Evaluation of BioPhotonic therapy in a non-healing diabetic foot ulcer: A case report. Diabetic Foot Canada 4: 25–30, 2016.

34. Carruthers J, Burgess C, Day D, Fabi SG, Goldie K, Kerscher M, **Nikolis A**, Pavicic T, Rho NK, Rzany B, Sattler G, Sattler S, Seo K, Werschler WP, Carruthers A. International Consensus Recommendations for Combined Aesthetic Therapies in the Face. Vancouver, WCD 2015. Dermatol Surg. 2016 May;42(5):586-97

35. Fabi SG, Burgess C, Carruthers A, Carruthers J, Day D, Goldie K, Kerscher M, **Nikolis A**, Pavicic T, Rho NK, Rzany B, Sattler S, Seo K, Werschler WP, Sattler G. Consensus Recommendations for Combined Aesthetic Interventions Using Botulinum Toxin, Fillers, and Microfocused Ultrasound

in the Neck, Décolletage, Hands, and Other Areas of the Body. Dermatol Surg. 2016 Oct;42(10):1199-1208

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39. **Nikolis A**, Grimard D, Pesant Y, Vezina D. A prospective case series evaluating the safety and efficacy of the KLOX BioPhotonic System in venous leg ulcers. Chronic Wound Care Management and Research, 2016:3 101-111

40. *Hamelin ND, **Nikolis A**, Armano J, Harris PG, Brutus JP. Evaluation of factors influencing confidence and trust in the patient-physician relationship: a survey of patient in a hand clinic. Chir Main. 2012 Apr;31(2):83-90.

41. *Suissa D, Danino A, **Nikolis A**. Negative-pressure therapy versus standard wound care: a meta-analysis of randomized trials. Plast Reconstr Surg. 2011 Nov;128(5):498e-503e. Review.

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43. **Nikolis A**, Tahiri Y, St-Supéry V, Landes G, Harris PG, Lessard L, Sampalis JS. Use of IV heparin in digital replantation and revascularization: The Quebec Provincial Replantation Program Experience. Microsurgery. 2011 Sep;31(6):421-7.

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47. *Dionyssopoulos AJ, **Nikolis A**, Papaconstantinou A, Kakas P, Milliaras D, Kekes G. Mucous cysts of the nose: a postrhinoplasty complication?: a long-term follow-up. Ann Plast Surg. 2010 Apr;64(4):381-4.

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49. *Cugno S, Rizis D, **Nikolis A**, Brutus JP, Cordoba C. Esophageal stricture and metaplasia following abdominoplasty. Aesthetic Plast Surg. 2010 Jun;34(3):388-91. Epub 2009 Jun 11.

50. *Tahiri Y, Bouteaud J, Tahiri M, Lessard L, Williams BH, **Nikolis A**. Routine drainage in reduction mammaplasty: an evidence-based analysis. J Plast Reconstr Aesthet Surg. 2010 Jun, 63(6), e549-50.

51. *Cugno S, Rizis D, **Nikolis A**, Brutus JP, Cordoba C. Esophageal Stricture and Metaplasia Following Abdominoplasty. Aesthetic Plast Surg. Aesthetic Plast Surg. 2010 Jun;34(3):388-91

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VII. COMMITTEES

- Director Aesthetic Surgery, Plastic Surgery, McGill University Residency Program (2019-)
- Pedagogical Committee, Plastic Surgery, McGill University Residency Program (2019-)
- Director Aesthetic Surgery, Plastic Surgery, University of Montreal Residency Program (2014-2018)
- Pedagogical Committee, Plastic Surgery, University of Montreal Residency Program (2016-2018)
- Continuing Medical Education Committee, Quebec Association of Plastic Surgery (2012-2014)
- Continuing Medical Education Committee, Quebec Association of Plastic Surgery (2008-09)
- Pedagogical Committee, Plastic Surgery Residency Program (2006-09, 2013-14)
- Admission Committee, Plastic Surgery Residency Program (2005-09, 2013, 2014, 2016)
- Plastic Surgery representative, CHUM Morbidity and Mortality committee (2007-09)

- Jury, Scientific Research Day, Department of Surgery, Université de Montréal (2007)
- Plastic Surgery Representative, Department of Surgery CHUM (2007-)
- Reviewer, European Journal of Plastic Surgery (2002-2004)
- Admission Committee, General Surgery, McGill University (1998)
- Admission Committee, Faculty of Medicine, Queen's University (1995)

VIII. ASSOCIATION-MEMBERSHIPS-POSITIONS

- Member, European Academy of Dermatology and Venereology
- Member, Canadian Society of Plastic Surgeons
- Member, American Society of Plastic Surgeons
- Member, Canadian Society for Aesthetic Plastic Surgery
- Member, Manus- Canadian Society for Surgery of the Hand
- Member, Quebec Association of Plastic and Aesthetic Surgery
- Executive member (Elected), Quebec Association of Plastic Surgeons (2007-2009)
- Associate Member, Canadian Association of General Surgeons (1996-2002)
- Member, Trauma Association of Canada (1998-2004)
- Member, Hellenic Medical Association of Quebec

IX. PEDAGOGICAL ACTIVITIES

- Aesthetic Surgery, Journal clubs. McGill University (2019-)
- Coordinator, Facial injectables course, resident series. (2012-)
- Journal Club Coordinator, Plastic Surgery residency program (2012- 15)
- Head and Neck Cadaveric Dissection Course: Université de Montréal (2012)
- President, Organizing committee, Canadian-Hellenic Congress (2009)
- Research Coordinator, Plastic Surgery Representative, Université de Montréal (2006-2009)
- Organizer, Plastic Surgery Teaching Rounds, Hôpital Notre Dame (2005-2009)
- Animal handling in experimentation course (2008)
- Assistant Professor, Plastic Surgery residency program (2004-2009)
- Associate Professor, Plastic Surgery residency program (2010-)
- Organizer Cadaveric Dissection Course: Université de Montréal (2006, 2007)
- Research Coordinator, Plastic Surgery residency program (2006-2009)
- Course Instructor, Introduction to the Clinical Patient (2004-2006)
- Craniofacial Surgery Rounds (2003-2006)
- Medical Student OSCE examination (1996-1999)

X. INVITED SPEAKER/COURSE INSTRUCTOR

- Masterclass 2021, Athens July 2021
- Think in IMCAS program, July 2021
- LMT France, May 2021
- India Complication avoidance, May 2021
- Australian Aesthetic meeting, May 2021
- GAIN China, April 2021
- LMT Greece, Jan 2021
- Australia Society Aesthetics April 2021
- China Innovations meeting, Nov 2020
- Nordics GAIN, Nov 2020
- GAIN Mexico, Oct 2020
- New Zealand Society of Cosmetic Medicine, Oct 2020
- 35th Annual meeting of the Spanish Aesthetic Society, Feb 2020
- Chair- IMCAS France, Jan 2020
- Chair- GAIN Montreal, Nov 2019
- Chair- GAIN Vancouver, Nov 2019
- Chair- LMT Thailand, Bangkok, Aug 2019
- Chair- Innovations Meeting, and LMT, Berlin, June 2019
- Lower face, Australia Tour, June 2019
- ICLO Cadaver course, Verona, Italy, May 2019
- LYFT Launch, Singapore, China, April 2019
- Chair- AMWC Monaco, April 2019
- Chair- IMCAS France, Jan 2019
- CAAM Canada, Nov 2018
- CLASS Canada, Nov 2018
- MAEXS Switzerland, Energy devices, Zurich, Switzerland. Sept 2018
- Global thought leader's meeting- Co-chair, Athens, Greece, June 2018
- GAIN meeting, Verona Italy- June 2018

- AMWC Asia, Taiwan - April 2018
- Chair- GAIN meeting Toronto, May 2018
- Cadaver dissection, Facial anatomy and injections. McGill Simulation Center Montreal, Jan. 2018
- Chair- IMCAS, Mastering the midface, Podium presentation (Chair) Jan. 2018
- LMT meeting, France, Nov. 2017
- CARAT meeting, UK, Oct. 2017
- Canadian Skinboosters Symposium, Toronto, April 2017
- LMT training course. Uppsala, Sweden, April 2017
- AMWC Podium presentation, Monaco, April 2017
- Dubai Derma Podium presentation, Dubai, March 2017
- Hellenic Dermatology Society Podium presentation. Delfous, Greece, April 2017
- Canadian LMT in facial aesthetics, Montreal, Nov 2016
- Cadaver dissection Facial anatomy and injections. McGill Simulation Center Oct Montreal, 2016
- Breast reconstruction, BRA Day, Montreal, Oct. 2016
- Skinboosters in facial rejuvenation. CSAPS Galderma Symposium Sept. 2016
- Jawline rejuvenation Canadian Association of Aesthetic Medicine, Toronto, Sept 2016
- Jawline rejuvenation American Association of Dermatology, Washington, Sept 2016
- Facial rejuvenation course. Andreas Syggros Hospital, Athens, June 2016
- Aging Caucasian Face. Bangkok, April 2016
- Facial rejuvenation. AMWC Monaco, April 2016
- Facial rejuvenation. Stockholm CMT, April 2016
- Wound healing. WCD Vancouver, Jan 2016
- Facial rejuvenation. Stockholm CMT, December 2015
- Facial rejuvenation with injectables and energy devices– Face to Face, France 2015
- Jawline rejuvenation. Redefining the need for a new lower face aging severity scale. Merz IMCAS (May 2013, Jan 2014)

- Wound healing– Copenhagen, Oct. 2015
- Biophotonics in a rat model, EWMA London UK, May 2015
- Treatment of grade II-III pressure sores with biophotonics. EWMA London UK, May 2015
- Reconstruction in the management of Cutaneous Melanoma.
    - Melanoma Symposium, Université de Montréal, May 2013
- Novel injection techniques using facial proportions. Allergan Academy. (April. 2012)
- University of Montreal Plastic Surgery residency - Course instructor on facial injectables (2012, 2013, 2014)
- Five-year outcomes following regionalization of microvascular replantation and revascularization surgery. ASCPEQ, Montreal, Québec, Feb, 2011
- How to prepare a fellowship application. Université de Montréal (2011, 2012)
- The use of the Fibonacci series in facial proportions. HMAQ Dec. 2010
- Breast reconstruction options following oncologic ablation. Journée de la femme, Montreal 2009
- The role of the Plastic Surgeon in the treatment of Melanoma.
    - Melanoma Symposium, Université de Montréal, Feb. 2008
- Hôpital Sacre Coeur Level I Trauma Center, Montreal, QC January 2008
    - Evolution of pain management in wound healing, Surgical Grand Rounds
- Trauma Défis, Quebec Association of traumatology in Emergency Medicine
    - Evolution of regional microsurgical trauma care, Quebec, March, 2008 Continuing Medical Education lectures
- North American Skull Base Society, Phoenix, Arizona, February 2006
    - The necessity of supportive services in Skull Base Surgery, Continuing Medical Education lectures
- Canadian Association of Wound Healing, Montreal, QC November 2005
    - The use of flap coverage in chronic wounds
- North American Skull Base Society, New Orleans, Louisiana, February 2004
    - Complications of Skull Base Surgery, Continuing Medical Education lectures
- North American Skull Base Society, Memphis, Tennessee, February 2003
    - Instrumentation in Skull Base Surgery, CME lectures

XI. PATENTS

- USE OF FILLER IN AMPUTATED EXTREMITIES TO SIMULATE SOFT TISSUE COVERAGE

  Publication number: 20200306459
  Abstract: Hyaluronic acid is used for simulating subcutaneous soft tissue in a residual limb of a subject.
  Type: Application
  Filed: March 25, 2019
  Publication date: October 1, 2020
  Inventor: Andreas Nikolis

- Tissue filler compositions and methods of use

  Patent number: 10772990
  Abstract: The present disclosure relates to methods for stimulating collagen synthesis, cosmetic enhancement of soft tissue and/or inhibiting or treating scarring comprising administering a composition to an area to be treated within a soft tissue, wherein the composition comprises a tissue filler medium and a fluorophore; and illuminating the area with light having a wavelength which can be absorbed by the fluorophore.
  Type: Grant
  Filed: December 20, 2018
  Date of Patent: September 15, 2020
  Assignee: KLOX TECHNOLOGIES INC.
  Inventors: Andreas Nikolis, Lise Herbert

- BIOPHOTONIC COMPOSITIONS COMPRISING A FUNGAL-DERIVED CHROMOPHORE

  Publication number: 20200222536
  Abstract: The present disclosure provides biophotonic compositions comprising one or more fungal-derived chromophores and methods useful in phototherapy. In particular, the biophotonic compositions and the methods of the present disclosure are useful for the treatment of rare diseases that afflict skin or soft tissues. The present disclosure also provides a photoactivatable fabric composition in combination with the biophotonic compositions.
  Type: Application
  Filed: May 23, 2017
  Publication date: July 16, 2020
  Inventors: Francesco BELLINI, Nikolaos LOUPIS, Remigio PIERGALLINI, Andreas NIKOLIS, Giovanni SCAPAGNINI

- TISSUE FILLER COMPOSITIONS FOR PHOTO-BIOMODULATION AND METHODS FOR ACHIEVING SAME

Publication number: 20200147214
Abstract: The present disclosure generally relates to photo-biomodulation composition comprising a tissue filler and to methods for achieving photo-biomodulation. Specifically, but not exclusively, the present disclosure relates to photo-biomodulation compositions which can be injected into a tissue for achieving photo-biomodulation.
Type: Application
Filed: July 18, 2018
Publication date: May 14, 2020
Inventors: Andreas NIKOLIS, Nikolaos LOUPIS, Remigio PIERGALLINI

- BIOPHOTONIC COMPOSITIONS AND METHODS FOR REDUCING SCARRING

Publication number: 20190224317
Abstract: The present disclosure relates to methods for reducing scarring of wounds. The methods comprising topically applying on the wound a biophotonic composition followed by illumination of the applied biophotonic composition with actinic light, wherein the method comprises the following schedule: (a) a period of from about 1 day to about 4 weeks during which, at least once every week the biophotonic composition is topically applied onto the wound and is illuminated for a period of at least 5 minutes, followed by a rest period of less than about a week; and (b) repeating step (a) over a period of at least 4 weeks.
Type: Application
Filed: September 22, 2017
Publication date: July 25, 2019
Inventors: Remigio PIERGALLINI, Nikolaos LOUPIS, Andreas NIKOLIS, Stéphane FAUVERGHE, Lise HEBERT, Francesco BELLINI

- TISSUE FILLER COMPOSITIONS AND METHODS OF USE

Publication number: 20190117844
Abstract: The present disclosure relates to methods for stimulating collagen synthesis, cosmetic enhancement of soft tissue and/or inhibiting or treating scarring comprising administering a composition to an area to be treated within a soft tissue, wherein the composition comprises a tissue filler medium and a fluorophore; and illuminating the area with light having a wavelength which can be absorbed by the fluorophore.
Type: Application
Filed: December 20, 2018
Publication date: April 25, 2019

Inventors: Andreas NIKOLIS, Lise HEBERT

- Tissue filler compositions and methods of use

  Patent number: 10207029
  Abstract: The present disclosure relates to methods for stimulating collagen synthesis, cosmetic enhancement of soft tissue and/or inhibiting or treating scarring comprising administering a composition to an area to be treated within a soft tissue, wherein the composition comprises a tissue filler medium and a fluorophore; and illuminating the area with light having a wavelength which can be absorbed by the fluorophore.
  Type: Grant
  Filed: April 1, 2015
  Date of Patent: February 19, 2019
  Assignee: KLOX TECHNOLOGIES INC.
  Inventors: Andreas Nikolis, Lise Hébert

- TISSUE FILLER COMPOSITIONS AND METHODS OF USE

  Publication number: 20170014549
  Abstract: The present disclosure relates to methods for stimulating collagen synthesis, cosmetic enhancement of soft tissue and/or inhibiting or treating scarring comprising administering a composition to an area to be treated within a soft tissue, wherein the composition comprises a tissue filler medium and a fluorophore; and illuminating the area with light having a wavelength which can be absorbed by the fluorophore.
  Type: Application
  Filed: April 1, 2015
  Publication date: January 19, 2017
  Inventors: Andreas Nikolis, Lise Hébert

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Acknowledgements

I would like to thank the individuals who have helped shape my course in academia. Professor Michael Koutsilieris who involved me in his laboratory in Quebec, Canada and allowed me to take part in my first research paper in 1991. Although he has since been geographically far, he remained «πνευματικά» close over the decades. Dr. John S. Sampalis who further developed my research skills in epidemiology and biostatistics as well as exposure to clinical research, leading to many years of collaboration and close friendship. To Professor Christina Antoniou who granted me access to Andreas Syggros hospital, and guided my course over these last several years, to Professor Panagiotis Skandalakis who allowed me to begin this project under his tenure, Professor Theodore Troupis who supervised the thesis, Professor Dimitrios Rigopoulos who extended my collaboration with the hospital and for the creation of new collaborations, and Professor Alexander J. Stratigos for his guidance and support. To my friend and colleague Professor Sebastian Cotofana who taught me that anatomy does not change over time, only our interpretation of it. On a personal note, to the people who are always behind you, those that support your every endeavor and have no doubt, even when you doubt yourself. Those that make it seamless because of all they do, there are no words to express my gratitude. Finally, to our patients who not only grant us the privilege of treating them, but also the opportunity to learn from them.

Abstract

Hyaluronic acid dermal fillers have been used to correct deformities of the temporal fossa caused by aging, by providing soft tissue augmentation and tissue support. While generally considered safe, adverse events (AEs) have been associated with these procedures. A thorough knowledge of the anatomy of the region, as well as an evaluation of the risks and benefits associated with different injection techniques are fundamental to ensuring optimal outcomes and avoiding AEs. In particular, the vasculature of the temporal region requires special attention as it can relate to serious AEs, such as arterial occlusion, ischemia, hematoma, and embolism. In this manuscript, the anatomy of the temporal fossa and how it relates to vascular AEs following filler injections will be reviewed. More specifically, the rarely studied Deep Temporal Arteries (DTA) will be evaluated given their minimally described anatomic placement as well as the clinical impact of bony changes associated with aging of the bony temporal fossa. The risks and benefits of various injection techniques will be explored, in the context of these new clinical findings.

Περίληψη

Τα ενέσιμα υαλουρονικού οξέος εφαρμόζονται για τη διόρθωση παραμορφώσεων του κροταφικού βόθρου που σχετίζονται με την ηλικία, παρέχοντας αύξηση μαλακών ιστών καθώς και υποστήριξη αυτών (ιστών). Αν και γενικά θεωρούνται ασφαλή, σημαντικές ανεπιθύμητες ενέργειες (ΑΕ) έχουν συσχετιστεί με χρήση αυτών. Η ενδελεχής γνώση της ανατομίας της περιοχής, καθώς και η αξιολόγηση των κινδύνων και τα οφέλη που σχετίζονται με τις διαφορετικές τεχνικές έγχυσης, είναι θεμελιώδεις για τη διασφάλιση βέλτιστων αποτελεσμάτων και την αποφυγή των ΑΕ. Ειδικότερα, η αγγείωση της κροταφικής περιοχής απαιτεί ιδιαίτερη προσοχή καθώς μπορεί να σχετίζεται με σοβαρές ΑΕ, όπως η αρτηριακή απόφραξη, ισχαιμία και εμβολή. Στα πλαίσια αυτά, διερευνήσαμε την ανατομία του κροταφικού βόθρου και τον τρόπο με τον οποίο σχετίζεται με τις αγγειακές ΑΕ ύστερα από ενέσιμα υαλουρονικού οξέος. Επιπλέον, εξαιτίας της έλλειψης δεδομένων στον τομέα της αισθητικής καθώς και των επιπτώσεων στις βαθιές κροταφικές αρτηρίες (deep temporal arteries), διερευνήσαμε και αξιολογήσαμε την ανατομία της περιοχής και την επίδραση αυτών των ενέσιμων θεραπειών επί των αγγείων.

Table of acronyms

Definition	Abbreviation
Adverse events	AEs
Body mass index	BMI
Computed tomographic	CT
Deep temporal artery	DTA
Facial lipoatrophy	FLA
Food and Drug Administration	FDA
Galderma Temple Volume Deficit Scale	GTVDS
High frequency ultrasound imaging	HFUI
Hollowness Severity Rating Scale	HSRS
Human immunodeficiency virus	HIV
Hyaluronic acid	HA
Inferior temporal septum	ITS
Lateral orbital fat compartment	LOFC
Lateral temporal cheek fat compartment	LTFC
Lower temporal compartment	LTC
Medial zygomaticotemporal vein	MZTV
Magnetic resonance imaging	MRI
Merz Temple Volume Scale	MTVS
Middle temporal artery	MTA
Middle temporal vein	MTV
Orbicularis retaining ligament	ORL
Poly-L-lactic acid	PLLA
Serious adverse events	SAEs
Superficial musculoaponeurotic system	SMAS
Superficial temporal artery	STA
Superior temporal septum	STS
Supraperiosteal superficial musculoaponeurotic system	Supra-SMAS
The facial nerve	TFN
Ultrasound	US
United States of America	US
Upper temporal compartment	UTC
Zygomatic cutaneous ligament	ZCL

Zygomatico-orbital artery ZOA

Preamble

Understanding of the temporal region remains difficult, largely because of ambiguous nomenclature, the multiplicity of names used for the same structure (e.g., no fewer than fourteen names have been used to describe the superficial temporal fascia), and the mislabeling of others.[1,2] Anatomical terminology in the temple is highly variable within the current body of literature, which has made this region difficult to describe. The use of consistent nomenclature to describe the structures in the temporal region facilitates understanding and discussion of the anatomy. Therefore, for the purposes of the current manuscript, the terms described in Box 1 will be used. Aside from difficulties with nomenclature, aspects of the anatomy also remain unclear and debated. For example, many authors use the classic description of the scalp layers (layer 1: skin; layer 2: subcutaneous tissue; layer 3: musculoaponeurotic (galea-aponeurotica); layer 4: loose areolar tissue; and layer 5: periosteum). However, this classification scheme is lacking accuracy for the temporal region anatomy.[3] Therefore, the ten-layer classification system described by Cotofana et al[4] will be used (Box 2).

Box 1

Terms Used in the Literature and Preferred Terms Used in the Current Manuscript

Terms used in literature	Select references	Term used in current manuscript	Layer Nº
Superficial temporal fascia	Abul-Hassan, von Drasek Ascher, & Acland, 1986 Schmidt, Pogrel, & Hakim-Faal, 2001 Yang, Yang, & Morris, 2011 Yang, Yang, & Morris, 2011	Superficial temporal fascia	3
Temporoparietal fascia	Hing, Buncke, & Alpert, 1988 Tzafetta & Terzis, 2010 Yang, Yang, & Morris, 2011		
Temporoparietalis fascia	Knize, 2001 Tuccillo, Jacovella, Zimman, & Repetti, 2007		
Temporal parietal fascia	Punthakee, Mashkevich, & Keller, 2010		
Temporal fascia	Lettieri, 2008 Lightoller, 1925		
Mesotemporalis	de la Fuente & Honig, 2005 Marino, 1963		
Suprazygomatic extension of the SMAS	Campiglio & Candiani, 1997 Micheli-Pellegrini, 1992		
Fascia pretemporalis	Hinderer, Urriolagoitia, & Vildosola, 1987		
Superficial temporoparietal fascia	Owsley & Agarwal, 2008		
Superficial temporal aponeurosis	De La Plaza, Valiente, & Arroyo, 1991		
Superficial temporalis fascia	Davison, Mesbahi, Clemens, & Picken, 2008		
Temporal SMAS	Mendelson, Muzaffar, & Adams, 2002		
Galeal temporal fascia	Lettieri, 2008		
Frontotemporal SMAS	De La Plaza, Valiente, & Arroyo, 1991		

Musculoaponeurotic (galea-aponeurotica) layer	O'Brien, Ashton, Rozen et al., 2013		
Deep fat		Deep fat	4
Loose areolar tissue	Yang, Yang, & Morris, 2011		
Subgaleal fascia	Carstens, Greco, Hurwitz, & Tolhurst, 1991 Davison, Mesbahi, Clemens, & Picken, 2008 Tolhurst, Carstens, Greco, & Hurwitz, 1991		
Innominate fascia	Accioli de Vasconcellos, Britto, Henin, & Vacher, 2003 Agarwal, Mendenhall, Foreman, & Owsley, 2010 Tellioglu, Tekdemir, Erdemli et al., 2000		
Submusculoaponeurotic fascia	Tolhurst, Carstens, Greco, & Hurwitz, 1991		
Subaponeurotic plane	Abul-Hassan, von Drasek Ascher, & Acland, 1986 Dutton, 1994 Stuzin, Wagstrom, Kawamoto, & Wolfe, 1989		
Subsuperficial fascia space	Moss, Mendelson, & Taylor, 2000		
Subgaleal plane	Heinrichs & Kaidi, 1998 Stuzin, Wagstrom, Kawamoto, & Wolfe, 1989		
Subaponeurotic areolar tissue	Kirolles, Haikal, Saadeh et al., 1992		
Merkel gap	Casanova, Cavalcante, Grotting et al., 1986		
Parotid-temporal fascia	Stuzin, 2010 Trussler, Stephan, Hatef et al., 2010		
Superficial temporal fat pad	Agarwal, Mendenhall, Foreman, & Owsley, 2010 Heinrichs & Kaidi, 1998 Hwang & Kim, 1999 Yang, Yang, & Morris, 2011		
Fibrofatty extension	Krayenbuhl, Isolan, Hafez, & Yasargil, 2007 Salas, Ziyal, Bejjani, & Sekhar, 1998		

Deep temporoparietal fascia	Myckatyn & Mackinnon, 2004		
Suprafascial fat pad	Coscarella, Vishteh, Spetzler et al., 2000		
Subgaleal fat pad	Ammirati, Spallone, Ma et al., 1993		
Superficial fat pad	Babakurban, Cakmak, Kendir et al., 2010		
Temporal parietal fat pad	Punthakee, Mashkevich, & Keller, 2010		
Deep temporal fascia	Ammirati, Spallone, Ma et al., 1993 Babakurban, Cakmak, Kendir et al., 2010 Mendelson & Jacobson, 2008 Yang, Yang, & Morris, 2011	Deep temporal fascia	5
Temporalis fascia	Baker & Conley, 1979 Campiglio & Candiani, 1997 Davidge, van Furth, Agur, & Cusimano, 2010		
Temporal fascia	Dempsey, Oneal, & Izenberg, 1995 Kahn, Wolfram-Gabel, & Bourjat, 2000 Kim & Matic, 2005 Stuzin, Wagstrom, Kawamoto, & Wolfe, 1989 Tremolada, Candiani, Signorini et al., 1994		
Temporal aponeurosis	Campiglio & Candiani, 1997 Hinderer, Urriolagoitia, & Vildosola, 1987 Micheli-Pellegrini, 1992		
Temporalis muscle fascia	Barton, 1997 Hing, Buncke, & Alpert, 1988		
Profound temporal fascia	Zhang, Yan, Qi et al., 2002		
Fascia temporalis profunda	de la Fuente & Honig, 2005		
Deep temporalis fascia	de la Fuente & Honig, 2005		
Superficial temporal fat pad	Agarwal, Mendenhall, Foreman, & Owsley, 2010 Kim & Matic, 2005 Salas, Ziyal, Bejjani, & Sekhar, 1998 Stuzin, Wagstrom, Kawamoto et al., 1990	Superficial temporal fat pad	6

	Yang, Yang, & Morris, 2011
Intermediate temporal fat pad	Accioli de Vasconcellos, Britto, Henin, & Vacher, 2003 Campiglio & Candiani, 1997 Hwang, Kim, & Chung, 2004
Intrafascial fat pad	Ammirati, Spallone, Ma et al., 1993 Lei, Gao, Xu et al., 2006
Intermediate fat pad	Babakurban, Cakmak, Kendir et al., 2010 Ridgway & Larrabee, 2010
Middle temporal fat pad	Accioli de Vasconcellos, Britto, Henin, & Vacher, 2003
Interfascial fat pad	Coscarella, Vishteh, Spetzler et al., 2000
Temporal fat pad	Kahn, Wolfram-Gabel, & Bourjat, 2000

Note: SMAS = Superficial musculoaponeurotic system. The terms used in the current manuscript and the numerical listing of layers is based of those described by Cotofana, Gaete, Hernandez et al., 2020.[4]

Box 2

Soft Tissue Layers of the Temporal Region

1. Skin
2. Superficial fatty layer
3. Superficial temporal fascia
4. Deep fat
5. Deep temporal fascia
6. Superficial temporal fat pad
7. Deep lamina of the deep temporal fascia
8. Deep temporal fat pad
9. Temporalis muscle
10. Periosteum

Note: From "Cotofana S, Gaete A, Hernandez CA, et al. The six different injection techniques for the temple relevant for soft tissue filler augmentation procedures - Clinical anatomy and danger zones. *J Cosmet Dermatol.* 2020;19(7):1570-1579".[4]

Introduction

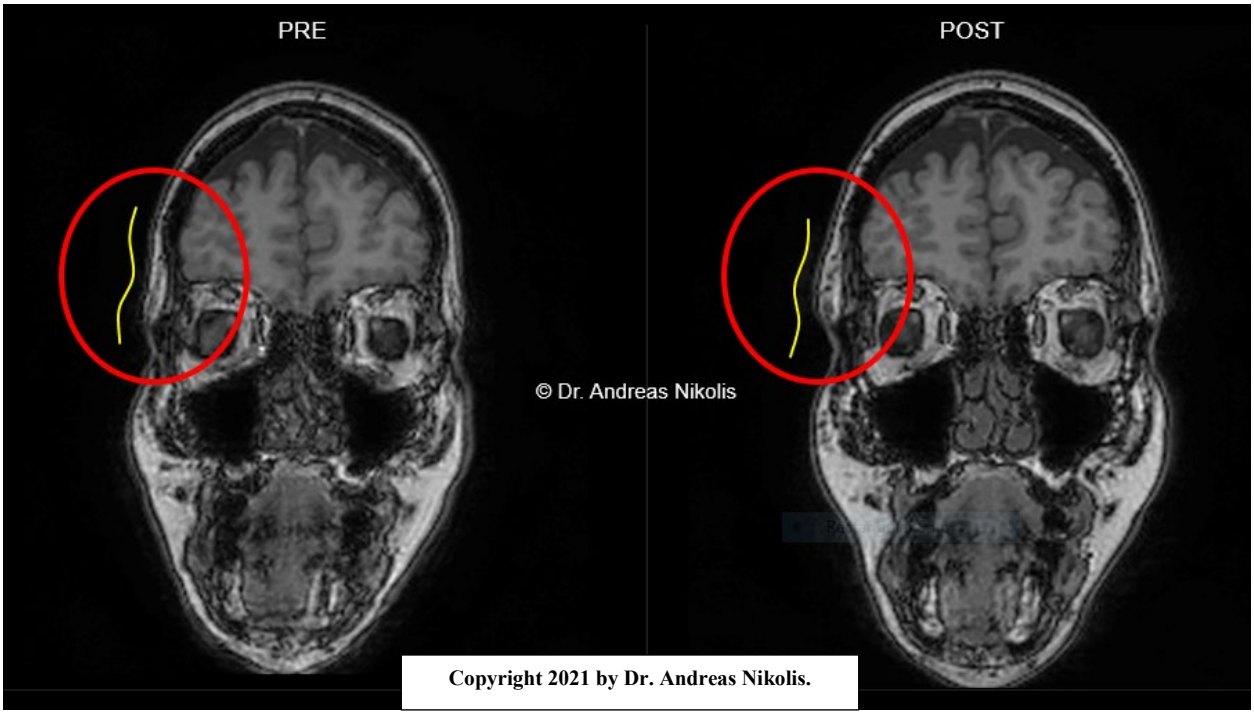
The physical evaluation of the aging face is based on changes of bone, soft tissues, and skin. These changes can be cosmetically improved by various surgical and non-surgical modalities. As minimally invasive procedures (e.g., injectable fillers) are becoming increasingly popular, the frequency of adverse events (AEs) associated with these procedures is proportionally increasing. To decrease these AEs, knowledge of anatomy is essential for their avoidance. The purpose of the present body of work is to identify existing anatomical considerations and expand on the aging process of the temporal fossa through i) assessment of the bony vault between genders and age, as well as ii) by identifying the anatomy and impact of lesser known and almost uniformly ignored deep temporal arteries (DTAs) of the temporal fossa. The ideal aesthetic result requires careful volumization of the temporal fossa, to alleviate hollowing and the skeletal appearance of the region (Figure 1), both of which contribute to lessening the aesthetic appearance of the upper face. With the help of magnetic resonance imaging (MRI) appropriate filler placement and the consequent change from a significant skeletal concavity to a more youthful and full appearance can be evaluated at the soft tissue level (Figure 2). To treat this issue, clinicians concentrate on treating the area of the temporal fossa that is anterior to the hairline. As such, volumes of injectable filler may reach 2 to 3mL per side. This equates to multiple needle sticks or cannulas entering the soft tissues in an anatomical area with significant danger zones. Avoidance requires meticulous technique married with extensive knowledge of anatomy, and sequential volumes of filler.

Figure 1
A female subject before (top) and after (bottom) augmentation of the temporal region with hyaluronic acid filler.

Figure 2

Magnetic resonance images of a female subject before (left) and after (right)

augmentation of the temporal region with hyaluronic acid filler.



Note: Same subject as depicted in Figure 1.

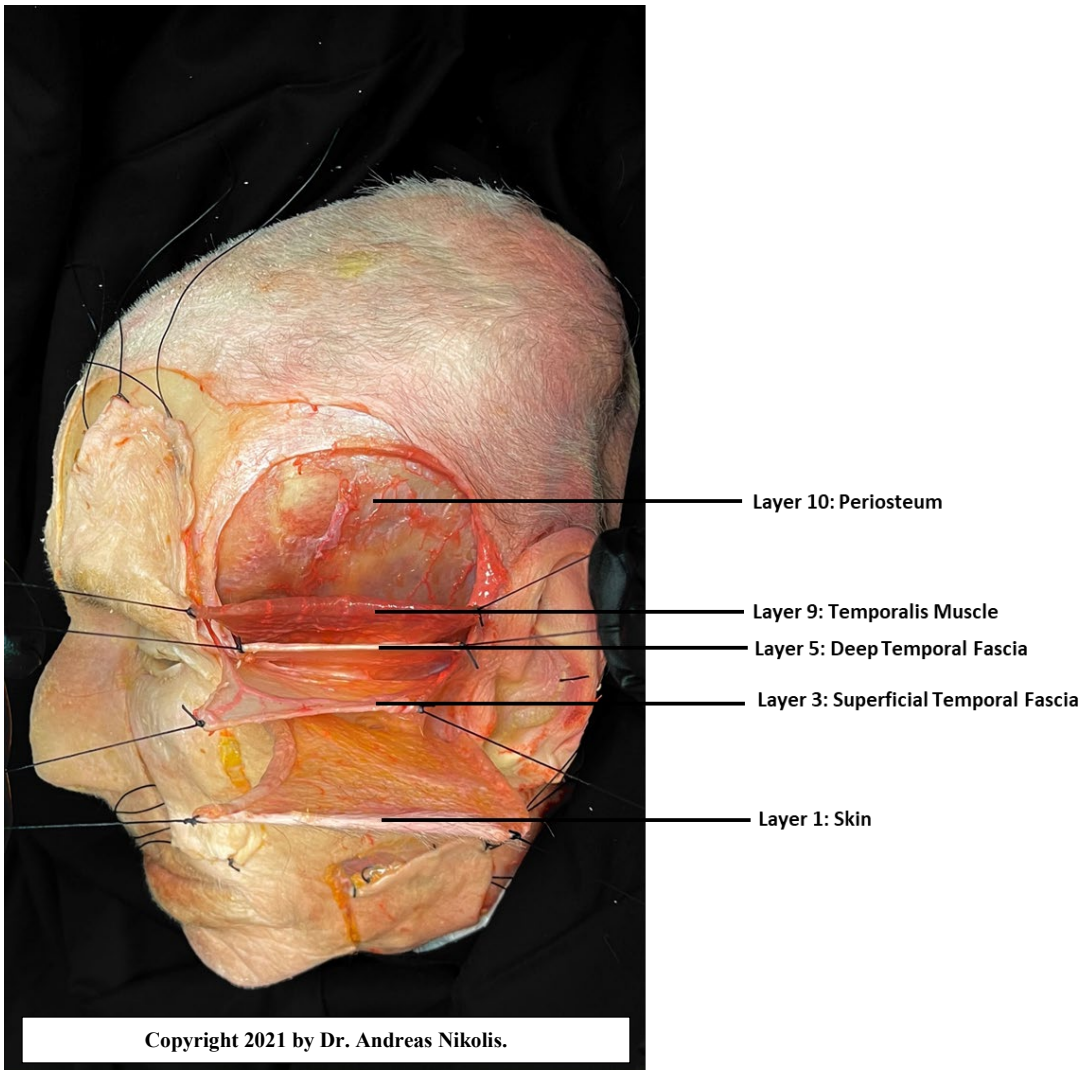
Temporal fossa anatomy

Tissue layers

Anatomically, the temporal fossa is a region of the upper face bounded inferiorly by the zygomatic arch, superiorly by the temporal line (i.e., linea temporalis), anteriorly by the processes of the zygoma and frontal bones and medially by the bones of the neurocranium. The temporal region is formed by the joining of the squamous temporal bone, the parietal bone, the greater wing of the sphenoid and the frontal bone at the pterion.[5] The temporal fossa sit on the squamous portion of the temporal bone above the zygomatic arch, beneath the periosteum, temporalis muscle and temporal fascia.[6] The superficial temporal fascia (temporoparietal fascia) is located beneath the skin and subcutaneous tissue, over the temporal fossa. A unified fascia layer from the scalp to clavicle is formed from the superficial temporal fascia, the superficial musculoaponeurotic system (SMAS) inferior to the zygomatic arch, and the platysma muscles in the neck. The superficial temporal fascia connects the orbicularis oculi and frontalis muscles anteriorly and the occipitalis muscle posteriorly.[7] The temporal crest, the bony ridge attaching the temporalis muscle, delineates the extent of the frontalis muscles in most people. The temporalis and masseter muscles form the two main closures of the jaw, responsible for crushing functions.[5] While somewhat debated, the layers of the temporal region include skin, superficial fascia, deep fascia, muscle, periosteum, and bone.[8] These layers can be viewed using post-mortem cadaveric dissection (Figure 3) or in living subjects via the use of non-invasive ultrasounds (US; Figure 4) and other imaging systems [(e.g., computed tomographic (CT)].

Figure 3

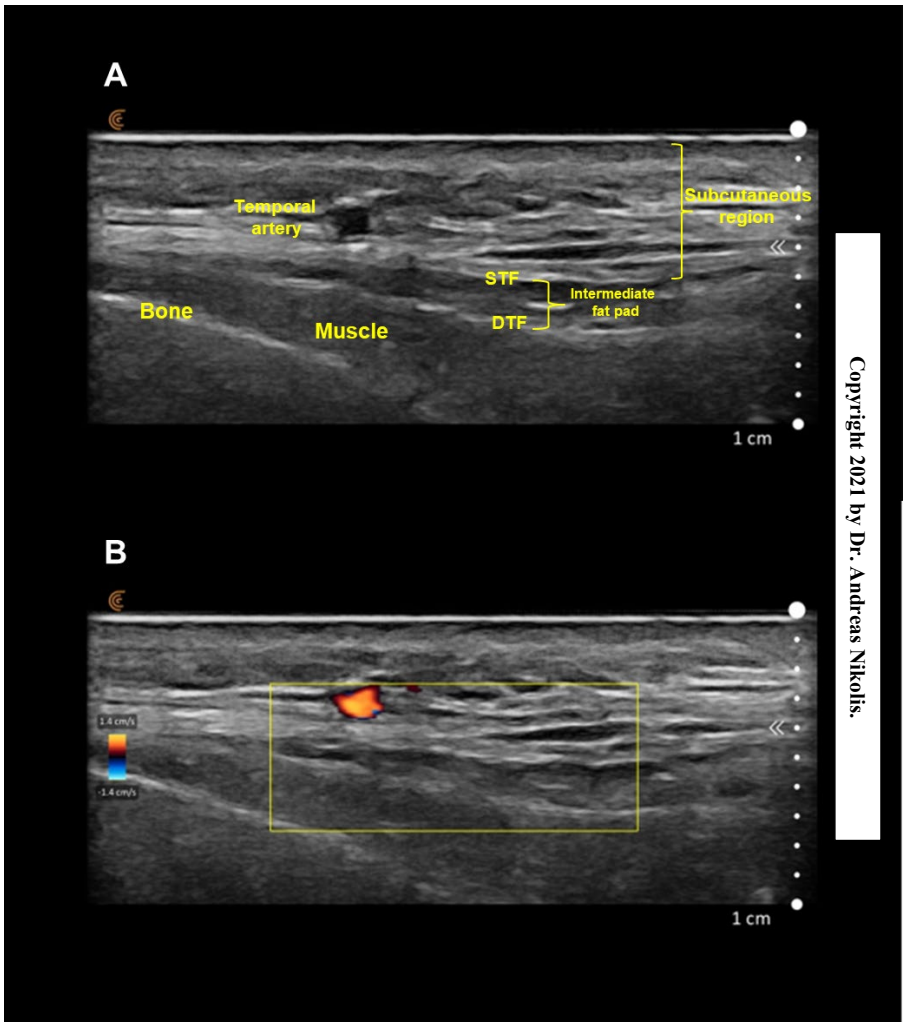
The Tissue Layers of the Temporal Region



Note: From superficial to deep, the major structures of the region include; skin, superficial temporal fascia, deep temporal fascia, temporalis muscle, and periosteum (note this dissection has the fat pads omitted). Copyright 2021 by Dr. Andreas Nikolis.

Figure 4

Non-Invasive Ultrasound Images of the Layers of the Temporal Fossa



Note: (A) Layers of the temporal fossa, as viewed using the brightness (B)-Mode of a non-invasive, ultra-high-frequency ultrasound (Manufacturer: Clarius; Model: L20 HD). (B) Color Doppler ultrasound displaying the speed and direction of blood flow within the temporal artery. The Color Doppler Function of an ultrasound displays flow towards the transducer in red and flow away from the transducer in blue. Lighter shades of color are assigned to higher velocities. STF = Superficial Temporal Fascia; DTF = Deep Temporal Fascia. Copyright 2021 by Dr. Andreas Nikolis.

Temporal hollowing refers to volume loss at the temporal fossa: the shallow depressions on either side of the forehead defined by the temporal lines, fusion line, lateral branch of the orbit, and zygomatic arch. Recent work has used three-dimensional (3D) CT imaging to quantify properties of the temporal fossa and identify differences in aging patterns based on gender, age, and body mass index (BMI).[9] As the temporal bone curved medially, the depth of the temporal fossa was determined by the temporalis muscle and temporal extension of the buccal fat pad. Independently from gender, age, and BMI, the deepest aspect of the temporal fossa was found to be located anteriorly and inferiorly. Overall, female subjects were found to have smaller anthropometric measurements compared to males. For example, the surface area of the temporal skin and bone, as well as the temporal soft tissue volume, were significantly smaller in female subjects (n = 30), compared to males (n = 28). Furthermore, while a significant reduction in temporal volume was associated with older age, this association was greater for females. In line with these findings, females seek treatment for temporal hollowing more frequently than males, even after considering their overrepresentation in aesthetic populations.

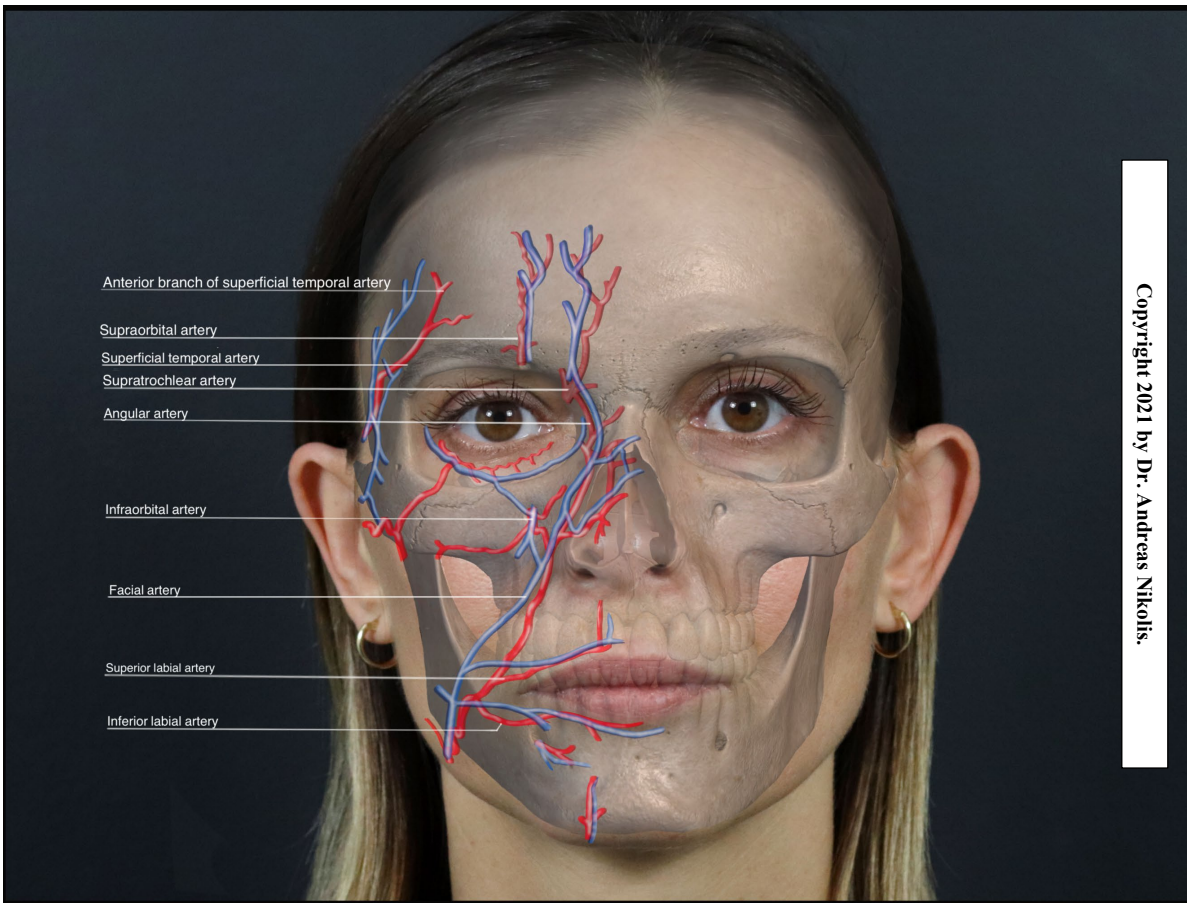
In the same study,[9] the authors identified increasing BMI to be associated with greater temporal soft tissue volume, but not greater temporal skin surface, in males. In females, the effect was inverted: increasing BMI was associated with greater temporal skin surface, but not greater temporal soft tissue volume. This observation is perhaps explained by differences in fat distribution between males and females. Based on these findings, males tend to accumulate more volume of fat in deeper layers whereas females accumulate volumes of fat in more superficial layers. Therefore, restoration of temporal

hollowing using dermal fillers may have the greatest aesthetic impact on older female patients affected by fat atrophy. However, these patients may also be at a greater risk of AEs; as atrophy of fat and muscles alters the ratio of soft tissue to vessels and increases the risk of vascular accidents. Injectors have developed and described various techniques to avoid the vasculature of the temporal fossa (see section entitled “Historical injection techniques”).

Vasculature

The three major vessels of the upper face (e.g., forehead, glabella, temporal fossa) include the supraorbital artery, supratrochlear artery, and the frontal ramus branch of superficial temporal artery (STA) (Figure 5). Vascular studies performed in thousands of patients have measured the positions of the arteries and identified countless variations and many classifications.[10-29] The main vascular anatomy of the temples consists of these major arteries: i) the superficial temporal artery, ii) the middle temporal artery, iii) the zygomatico-orbital artery, and iv) the DTAs. The associated veins typically follow their arterial counterparts. All major arteries of the temporal region are branches of the external carotid artery. These arteries can anastomose with the ophthalmic artery, imparting risk of blindness if they are inadvertently injected with filler.[30]

Figure 5
Major Vessels of the Upper Face

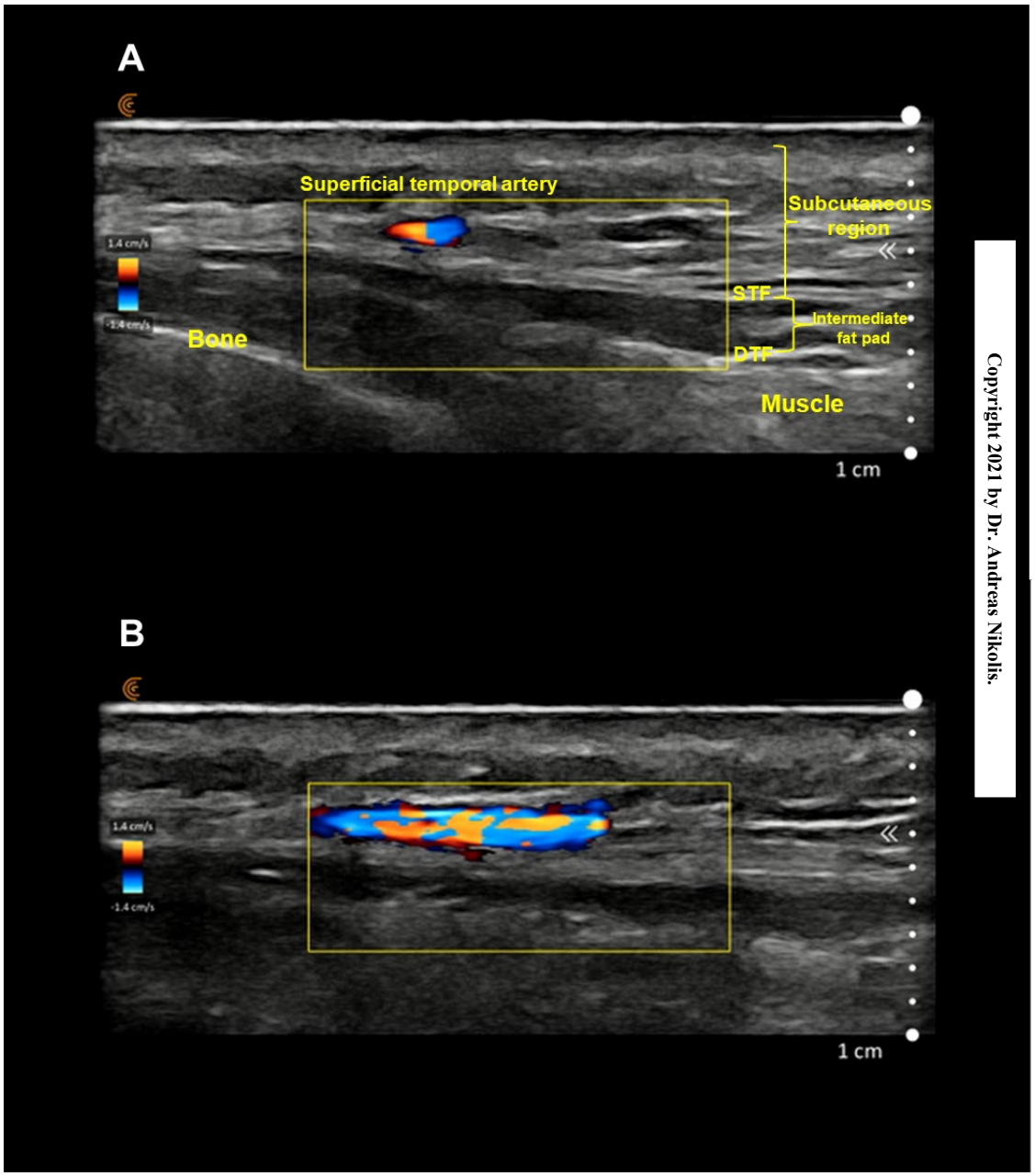


The superficial temporal artery (STA) and vein

The STA is a terminal branch of the external carotid artery, and it supplies the temporal, parietal, and sometimes the occipital areas.[31,32] The STA and vein lie in the subcutaneous plane just above the temporoparietal fascia (Figure 6). Injection techniques recommended for the temporal region frequently consider identifying and avoiding the STA,[23,33,34] as it is frequently implicated in cases of blindness resulting from temporal rejuvenation. As the pulse of the STA is often palpable, it has been recommended that injectors should first palpate the temporal region to locate the STA, prior to injection, to avoid accidental intra-arterial.[31] In some patients, the arterial pulsations are visible upon examination.[25] However, even with the use of palpation, as the position of the STA varies, it may be difficult to locate all branching channels.[21,24] The STA separates into anterior, middle (parietal) and sometimes, posterior (occipital) branches (Figure 7). These channels, especially that of the anterior branch (Figure 8), must be considered when performing injections as filler material may reach the ophthalmic artery via the external carotid artery system. Four different variations of the course of the STA, including bifurcations, have been described.[21,31] Compared to the anterior branch of the STA, the middle and posterior branch are less of a concern when performing temporal injections, given their more dorsal location on the scalp and behind the hairline, where volumization by filler would not offer any measurable aesthetic result.

Figure 6

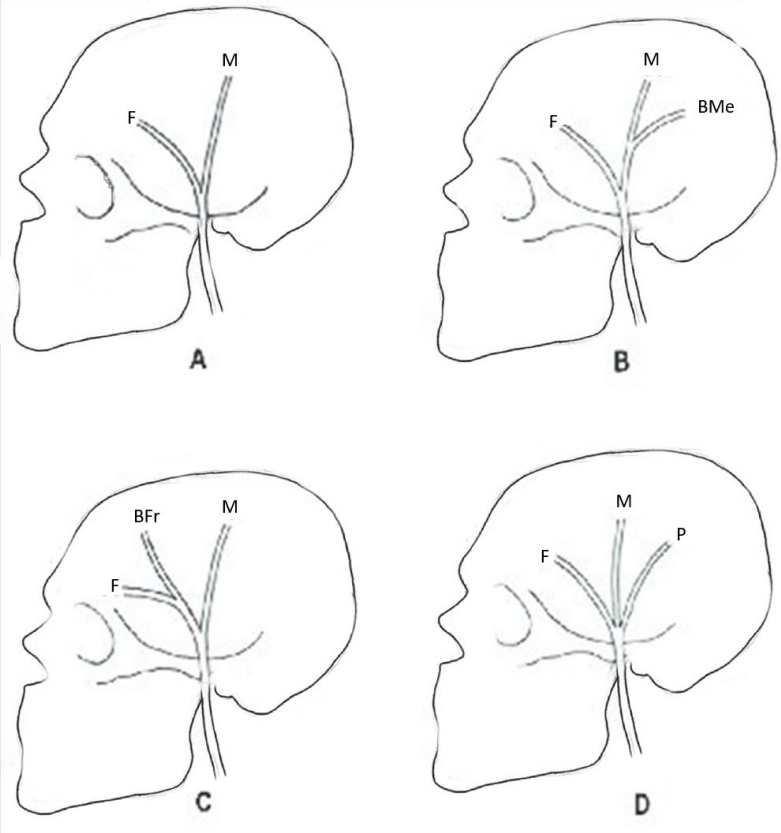
Doppler Ultrasound Images Displaying the Superficial Temporal Artery and Vein Laying in the Subcutaneous Plane, Just Above the Temporoparietal Fascia



Note: Image "A" displays the appearance of the artery when the ultrasound technician holds the device vertically and "B" displays the appearance of the artery when held horizontally. Copyright 2021 by Dr. Andreas Nikolis.

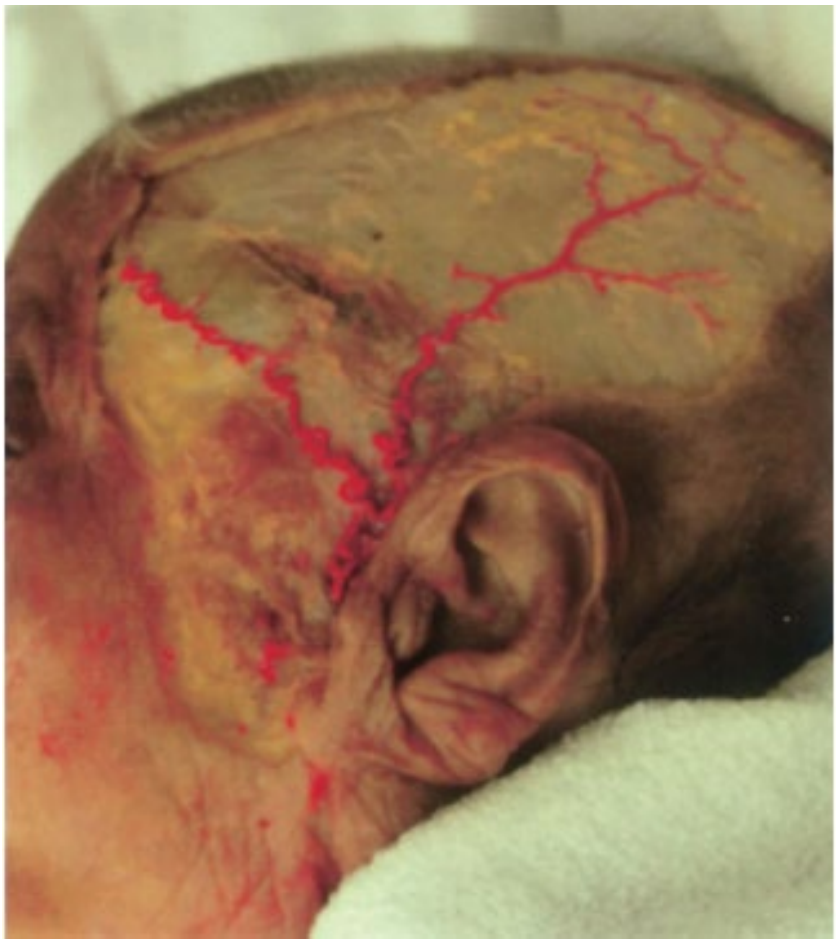
Figure 7

Observed Branching Patterns of The Superficial Temporal Artery



Note: A. Classical bifurcation into frontal (F) and medial (M) branches; B. Bifurcation of the medial branch (BMe); C. Bifurcation of the frontal branch (BFr); D. Trifurcation into frontal, medial and posterior (P) branches. “Frontal” is used interchangeably with “anterior”. Adapted from “Superficial Temporal Artery Among Kenyans: Pattern of Branching and its Relation to Pericranial Structures,” by P. Mwachaka, S. Sinkeet and J. Ogeng’o, 2010, *Folia Morphologiica, 69*(1), 51-53.[32]

Figure 8
Anterior and Middle Branches of the Superior Temporal Artery

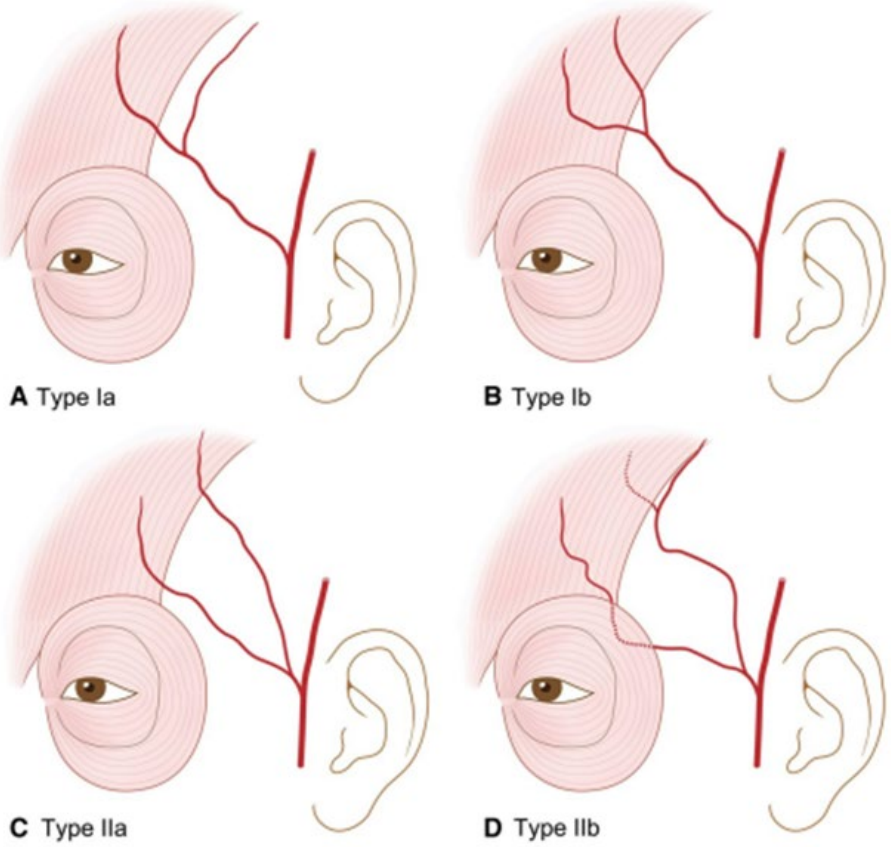


Note: From “Superficial Temporal Artery as an External Landmark for Deeper-Lying Brain Structures,” by Tubbs, O’Neil, Key et al., 2007, *Clinical anatomy (New York, N.Y.), 20*(5), 498-501 (https://doi:10.1002/ca.20363).[24]

In a cadaveric study of thirty-eight Korean (twenty-six males and twelve females; mean age 71.9 years) dissections, the location, and course of the anterior STA bifurcations were identified with reference to the lateral border of the occipitofrontalis muscle (Figure 9).[31] Investigators found that the ramification of the anterior STA occurred 36.9mm (SD: 14.24) superior and 17.2mm (SD: 8.2) anterior to the posterior point of the tragus. The anterior STA was observed as a single branch in most cases (i.e., 96.9 %). Its final destination was 14.8mm (SD: 7.7) superior to the uppermost point of the eyebrow and 15.8mm (SD: 9.1) from the lateral epicanthus. The diameter of the anterior STA was approximately 1.6mm (SD: 0.5). The authors conclude that clinicians performing injections within the temporal area should be aware of the various distributions of the anterior STA, as it is vulnerable to damage by fillers and neurotoxins.[31]

Figure 9

Classification of the Bifurcation Patterns of the Anterior Branch of the STA



Note: Images A-D are typical images for each type. From "Frontal Branch of the Superficial Temporal Artery: Anatomical Study and Clinical Implications Regarding Injectable Treatments," by Lee, Yang, Hu et al., 2015, *Surgical and Radiologic Anatomy, 37*(1), 61-68 (https:// doi:10.1007/s00276-014-1306-6).[31]

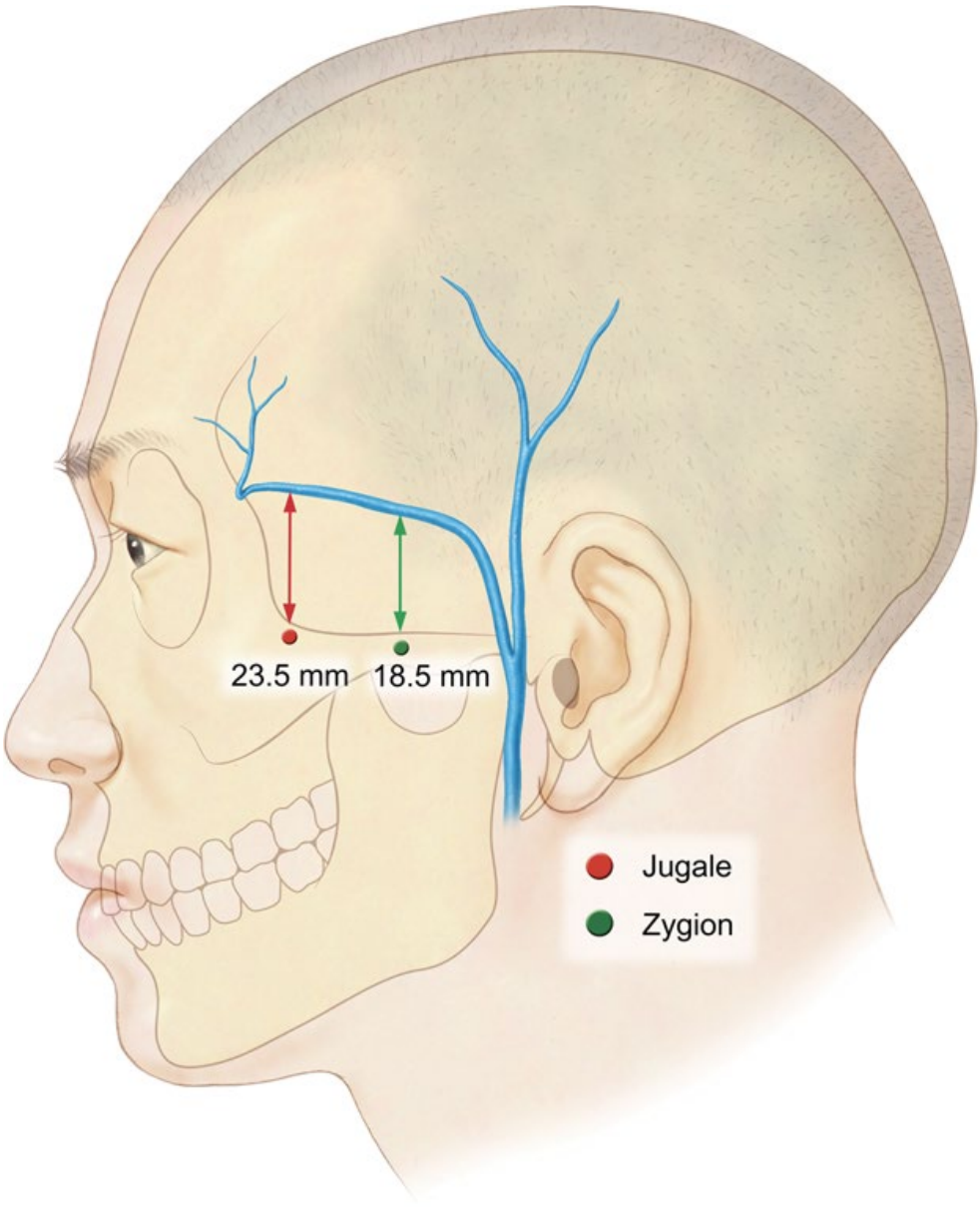
The middle temporal artery (MTA) and vein (MTV)

The morphology of the MTA has been reported by several authors.[28,29,35-38] The origin of the MTA is just anterior to the external acoustic meatus,[39] which provides injectors with a major anatomical landmark to identify this artery. The MTA arises from the frontal branch of the STA, crosses the zygomatic arch or 1-2cm above it, then enters the temporal fascia.[37] Before entering the temporal fascia, the branches of the MTA are unspecified and vary between studies, which suggests a complex branching pattern. Recently, Sakamoto[37] proposed that this variation may relate to the morphology of the STA. Jung et al[40] extensively studied the location of the associated MTV by evaluating eighteen hemifaces from nine Korean cadavers and measuring the distance between the MTV and the zygomatic arch. Authors concluded the distance to be approximately one fingerbreadth above the zygomatic arch (Figure 10), resulting in a safe injection zone using a thumb-width rule above the superior border of the zygoma (Figure 11). No main trunk of the MTV was found within this zone for any of the specimens assessed, concluding it to be the safest region for filler injection in temporal fossa augmentation. Other authors have recognized this safe filler zone and suggested further parameters including it to lie inferior to the superficial temporal vascular arcades and above the median temporal vein, with 1cm posterior along the temporal fusion line and 1cm inferior to this point and a pre-periosteal injection depth (Figure 12).[34,41] The MTV can also be used as an aid in locating the MTA, because the vein lies external to the artery and is often easier to find. The course and tributaries of the MTV drain directly into the internal jugular vein. This pathway, plus its relatively large diameter (i.e., up to 1cm), make the

MTV particularly vulnerable to intravascular injection, with the potential for emboli if accidentally injected with filler.[40]

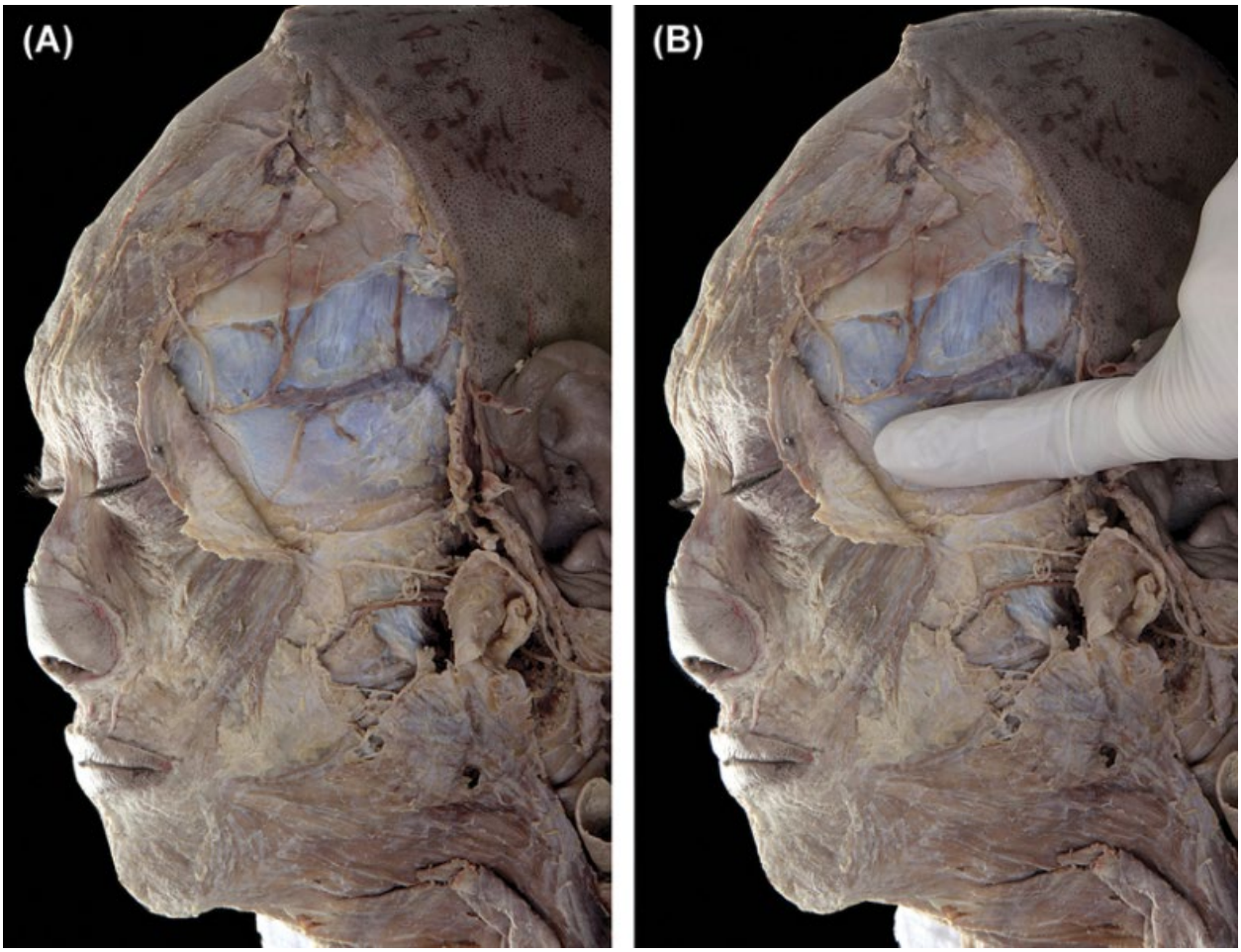
Figure 10

Distance Between the Middle Temporal Vein and the Zygomatic Arch



Note: From “Clinical Implications of the Middle Temporal Vein With Regard to Temporal Fossa Augmentation,” by Jung, Youn, Won et al., 2014, *Dermatologic Surgery, 40*(6), 618-623 (https://doi:10.1111/dsu.0000000000000004).[40]

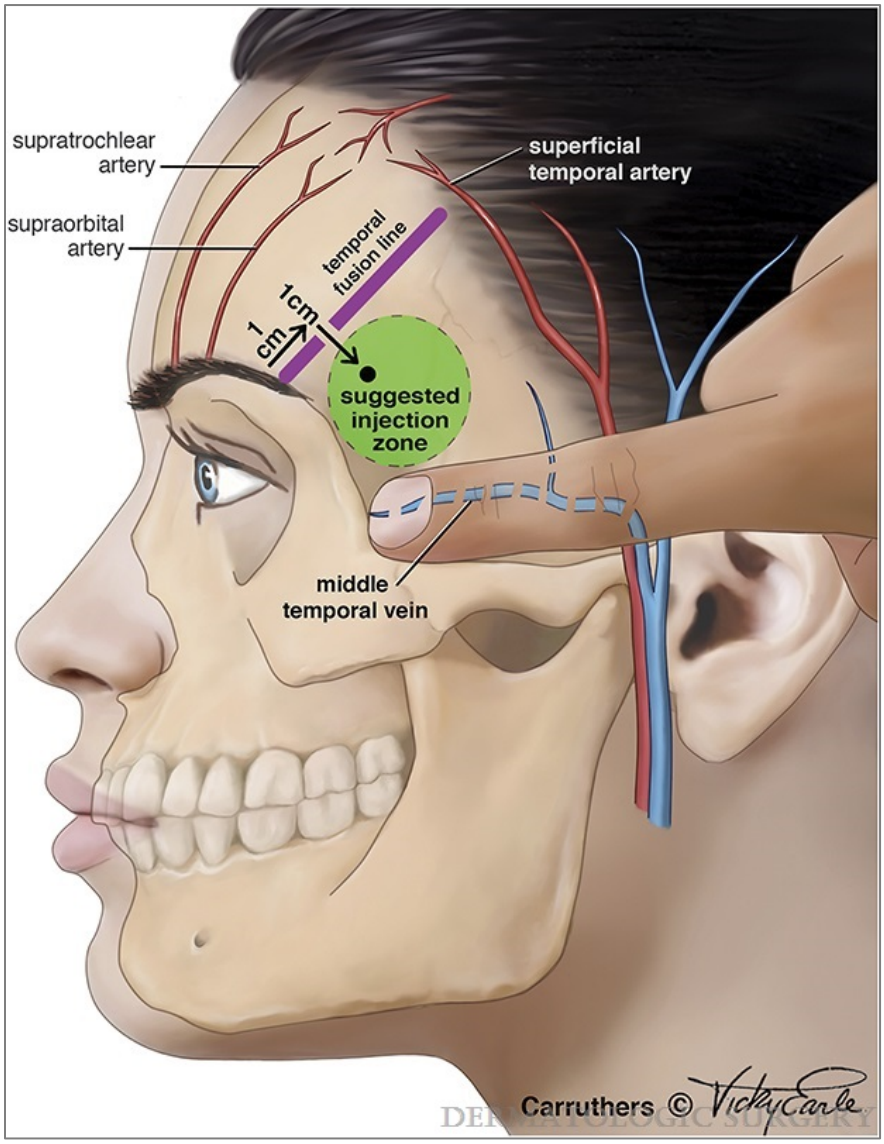
Figure 11
The Suggested Area for Safe Filler Injection



Note: The area suggested by Jung, Youn, Won et al. (2020) as being safe for filler injection, as no main trunk of the MTV was found in the area one finger width above the zygomatic arch in any of the specimens. Photographs of the MTV without (A) and with (B) a finger on the temple area. From “Clinical Implications of the Middle Temporal Vein With Regard to Temporal Fossa Augmentation,” by Jung, Youn, Won et al., 2014, *Dermatologic Surgery, 40*(6), 618-623 (https://doi:10.1111/dsu.0000000000000004).[40]

Figure 12

Suggested Safe Injection Zone for Avoiding the Middle Temporal Vein



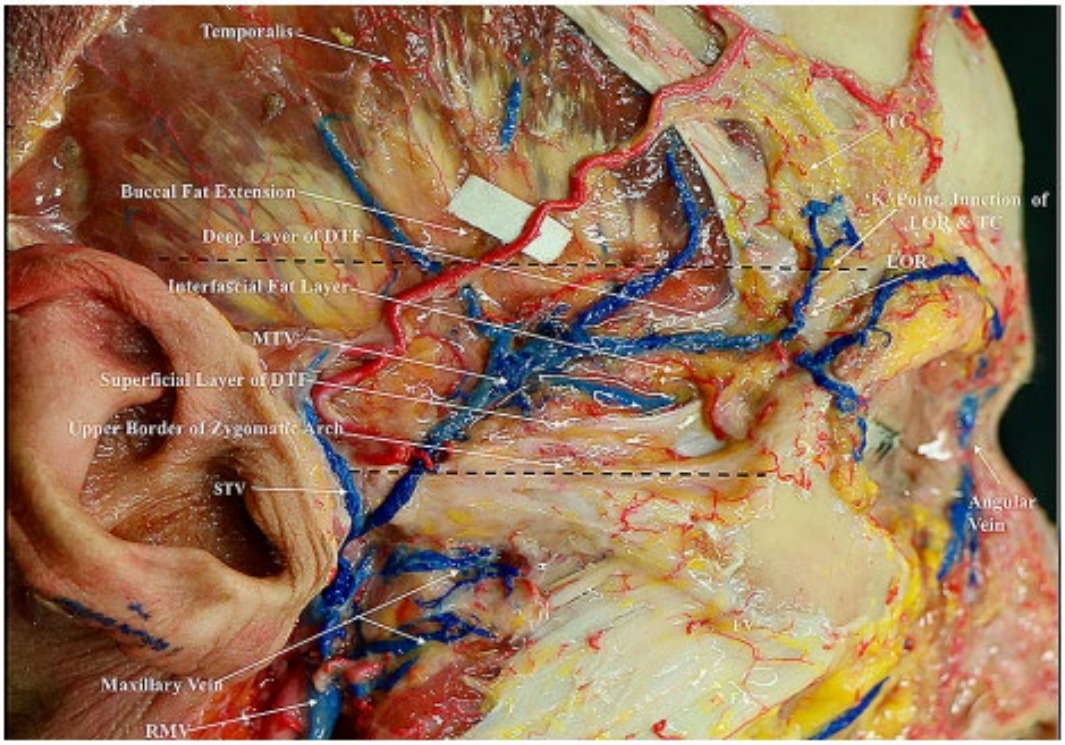
Note: The suggested safe injection zone for avoiding the middle temporal vein in the temporal region lies between the superolateral bony orbital margin, approximately 1cm inferior to the temporal fusion line and over one finger breadth above the superior border of the zygoma. From “Suggested Injection Zone for Soft Tissue Fillers in the Temple?” by J. Carruthers, S. Humphrey, K. Beleznay and A. Carruthers, 2017, *Dermatologic Surgery, 43*(5), 756-757 (https:// doi:10.1097/DSS.0000000000001057).[34]

The MTA and MTV lie just below the superficial vessels, in the space between the superficial layer of the deep temporal fascia and the temporoparietal fascia.[28,33] Relating to its size, position, course, tributaries and termination, the MTV is susceptible to accidental filler injection;[28,29,35,38] with pulmonary embolism having been reported following filler injections to correct temporal hollows.[38,42,43] When the MTV is accidentally injected with filler, the bolus follows the direction of blood flow in an anterograde fashion, towards the pulmonary artery. In rare cases, this mechanism can lead to embolism.[42,43] To assess risks of accidental MTV injection, investigators conducted a cadaveric anatomical study, wherein they performed 1) anterograde injections to assess the possibility of pulmonary embolism and 2) retrograde injections to identify outcomes such as venous rupture.[38] Anterograde injections of saline into the MTV via a cannulated tube towards the internal jugular vein resulted in a continuous flow of saline, revealing a direct channel from the MTV to the internal jugular vein. However, vascular compression at the preauricular venous confluent point against the zygomatic process successfully decreased the saline flow rate and resulted in a temporary cessation. Pressing on the retromandibular vein also resulted in sudden retardation of saline flow while compression of the facial vein showed no effect. Overall, the authors recommended temporary compression of the pre-tragal vascular confluent point during temporal injection to help minimize the risk of embolization. When the venous system did not rupture, retrograde injections did not lead to filler material passing through tributaries of the MTV into the opthalmic veins.

Despite an awareness of the MTV's existence being essential to mitigating undue vascular complications during aesthetic injections in the temporal region,[36] it is not a very

well-known vessel among clinicians.[36,40] To help injectors perform safer temporal fossa filler injections, a recent literature review aimed to delineate the “venous danger zone” of the temporal region, by providing detailed information about the course, depth, and size of the MTV.[36] Their review revealed that while the MTV displays a consistent course and depth in the temporal region, its diameter varies widely (i.e., 0.5mm to 9.1mm). It was found that the MTV receives many subfascial tributaries from the surface of the temporalis muscle, and runs mostly in the fat pad, enclosed between superficial and deep layers of the deep temporal fascia. This led the authors to propose the presence of a “venous danger zone” (Figure 13) in the inter-fascial planes of the temporal fossa, which contains the main part of the MTV and its tributaries.[36] The authors discovered that the location of the MTV can be identified in relation to the superior border of the zygomatic arch, which can be easily palpated with a fingertip, and the zone of the MTV can be marked above the zygomatic arch. Based on their analysis of the course of the MTV, the highest density of perforations was found up to 35mm above the zygomatic arch. Therefore, they proposed that the danger zone for performing temporal fossa augmentation with fillers extends to at least 34mm above the zygomatic arch, due to the variable position (-2 to 25mm from the upper border of the zygomatic arch), oblique course, and large size of this vessel. Therefore, the earlier suggested “safest area” (at one finger width above the zygomatic arch)[34] was found to be unsafe by Kapoor et al.[36]

Figure 13
The Proposed Venous Danger Zone



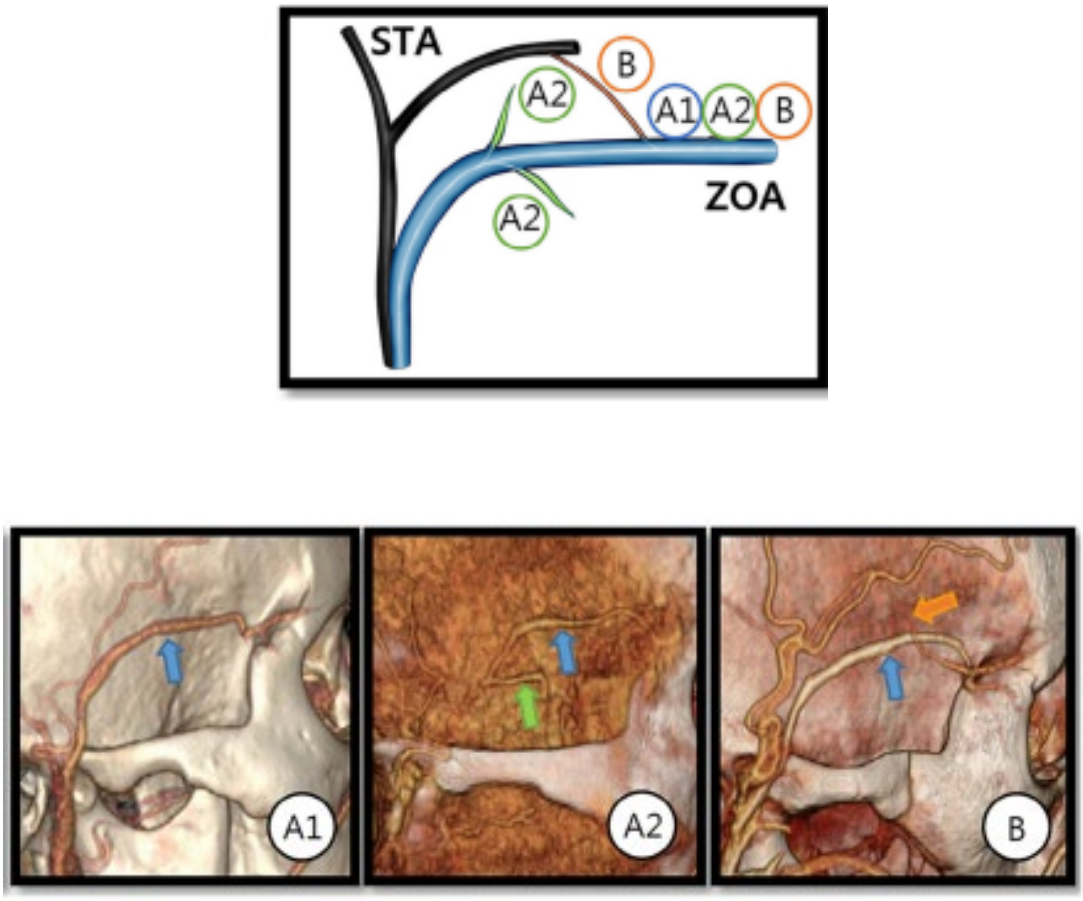
Note: Proposed "venous danger zone" in the temporal fossa, marked between the upper border of the zygomatic arch and an imaginary horizontal line drawn from the junction point ("K Point") between the lateral orbital rim and temporal crest. From "A Systematic Literature Review of the Middle Temporal Vein Anatomy: 'Venous Danger Zone' in Temporal Fossa for Filler Injections," by Kapoor, Bertossi, Li et al., 2020, *Aesthetic Plastic Surgery, 44*(5), 1803-1810 (https://doi:10.1007/s00266-020-01791-2).[36]

The zygomatico-orbital artery (ZOA)

Despite being the largest artery in the temporal area, with a mean diameter up to 2.52mm, the anatomy of the zygomatico-orbital artery (ZOA) has rarely been studied in relation to filler injections.[44,45] The ZOA forms from the external carotid artery, as the main branch of the MTA; and runs parallel to the upper zygomatic arch. Subsequently, it runs horizontally toward the lateral canthus and transfers to the palpebral and superficial orbital arteries.[46,47] The ZOA overlaps with the temporal branch of the facial nerve 1 to 3cm posterior to the lateral canthus. Unlike the other main arteries of the temporal region, investigators have been unable to locate a concomitant vein associated with the ZOA.[45] Based on the results of an anatomical study in fifty patients who underwent CT imaging, the branching pattern of the ZOA was classified into three types, depending on its bifurcation and relationship with other arteries. Subtype A1 runs toward the lateral canthus without bifurcation; A2 bifurcates once or twice in the main course toward the lateral canthus; and Type B formed an additional anastomosis with an adjacent artery (Figure 14). Authors have suggested that before performing injections, injectors should locate the ZOA by palpating the zygomaticofrontal suture and identifying the arterial pulse approximately 1cm posterior to the corresponding area. Alternatively, US may be used to non-invasively determine the location of this large vessel.[48]

Figure 14

Detailed Course of the Zygomatico-Orbital Artery, With Classification and Diagram of the Arterial Subtypes (Types A1, A2, And B)

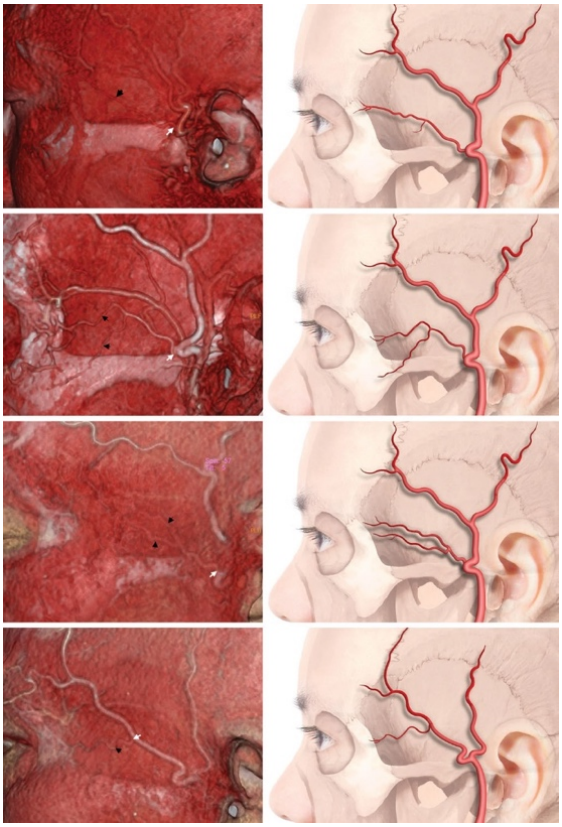


Note: Subtype A1 runs toward the lateral canthus without bifurcation (blue arrow); A2 bifurcates once or twice in the main course toward the lateral canthus (green arrow); and Type B forms an additional anastomosis with an adjacent artery (orange arrow). STA = Superficial temporal artery; ZOA = Zygomatico-orbital artery. From "Zygomatico-orbital Artery: The Largest Artery in the Temporal Area," by Choi, Eom, Lee et al., 2018, *Journal of Plastic, Reconstructive & Aesthetic Surgery, 71*(4), 484-489 (https://doi.org/10.1016/j.bjps.2017.10.003).[45]

Another classification pattern for the branching of the ZOA was recently proposed, based on findings from fifty-eight patients who underwent head contrast-enhanced 3D computed tomography and an investigation of ten fresh frozen cadavers.[49] It was observed that the majority (i.e., 94%) of ZOAs derived directly from the STA, with the remaining arteries starting from the anterior branch of the STA. According to its origin, the ZOA was classified into type I or II, with Type I being further classified into three subtypes. The trunk of the ZOA was located between the deep temporal fascia and the superficial temporal fascia, with deep branches piercing the superficial layer of the deep temporal fascia. The ZOA was noted to originate from 11.3mm anterior to the midpoint of the apex of the tragus, with most of its trunks being located $\leq$ 20.0mm above the zygomatic arch. The mean diameter of the ZOA was found to be smaller than in other samples,[44,45] at 1.2mm (SD: 0.2), and it had extensive anastomoses with various periorbital arteries at the lateral orbital rim (Figure 15). The authors maintained that when injecting filler into the layer between the deep and superficial temporal fascia, caution should be taken to avoid the ZOA.[49]

Figure 15

Distribution Patterns of the Zygomatico-Orbital Artery



Note: Type I (above, second from above, and second from below) refers to zygomatico-orbital arteries originating from the superficial temporal artery, and type II (below) refers to zygomatico-orbital arteries originating from the frontal branch of the superficial temporal artery running toward the lateral orbital rim. (Above) Type Ia arteries have one trunk running obliquely to the lateral orbital rim. (Second from above) Type Ib arteries divide into two branches above the midpoint of the zygomatic arch, both of which run to the lateral orbital rim at an angle. (Second from below) Type Ic arteries divide into two branches near the root of the zygomatic arch, both of which run parallel to the lateral orbital rim. The white arrow indicates the origin of the zygomatico-orbital artery. From "Topographic Anatomy of the Zygomatico-Orbital Artery: Implications for Improving the Safety of Temporal Augmentation," by Liu, Yan, Wang et al., 2021, *Plastic and Reconstructive Surgery, 148*(1), 19e-27e.[49]

The deep temporal arteries (DTAs)

While there have been published studies to describe the STA and MTA, there is limited information about the location and course of the DTAs. The DTAs have been described to run along the periosteum of the skull, with some branches communicating with the MTA at the center of the temporal region. Together, the DTAs and MTA supply blood to the temporalis muscle.[33,44] One study located the anterior branch of the DTA intramuscularly,[50] while a cadaveric study evaluating fifty-six Chinese heads using CT imaging found the posterior branch of the DTA arose from the maxillary artery and ran into the temporal region at the midpoint of the zygomatic arch, at a depth of 14.13mm (SD: 6.26mm). From this point, the branches of the DTA ran directly upwards.[44] As these two studies investigated only single branches of the DTA, it remains unclear if, like other major arteries, the DTA may consist of anterior, middle, and posterior branches. Moreover, the varied distribution patterns of the DTA and frequency of bifurcations remains to be elucidated.

Other important structures of the temporal region:

The medial zygomaticotemporal vein (MZTV)

While AEs resulting from intravascular injection of arteries are often more severe than those arising from accidental injection into veins, they can still lead to signs and symptoms that are disturbing to patients, such as bruising, pain, and migraines.[51,52] One such example is a tributary of the ZOA: the medial zygomaticotemporal vein (MZTV). The MZTV is a perforating vessel that passes through the temporoparietal fascia and

superficial layer of the deep temporal fascia. It gathers blood around the lateral orbital rim and drains it into the MTV and ultimately, the STV.[53] The MZTV is consistently observed to be located closely to the temporal branch of the facial nerve, and as such, the MZTV has been recognized as an important landmark for avoiding this nerve during procedures in the lateral orbital area. Given its importance as an anatomical landmark, the MZTV has been referred to as “the sentinel vein”.[28,54,55]

The temporal branch of the facial nerve (TFN)

The temporal branch of the facial nerve (TFN) lies within the superficial temporal fascia and/or the areolar tissue just beneath the superficial temporal fascia.[56] The TFN often accompanies the STA and as such, the STA has been suggested as an anatomical landmark for locating the TFN.[57] The anatomical relationship between the TFN and STA has been studied in cadavers to help define a safe plane for preservation of the frontotemporal branch of the TFN.[58,59] Using layer by layer dissection, investigators found that the TFN lies deep within the temporoparietal fascia and superficial fat pad, with branches anteroinferior to the STA (which travels in a superficial plane of the temporoparietal fascia). Moreover, three distinct branches of the TFN were found within the galeal plane: the auricularis, frontalis and orbicularis rami.[59,60] Further cadaver analyses have identified the distribution of temporal branches of the facial nerve with relation to the orbicularis oculi, showing subbranches commonly sent from the temporal branch into the orbicularis oculi on the zygomatic arch.[61] Specifically, the lowermost subbranch forms a neural plexus with the subbranch of the zygomatic branch prior to entering the orbicularis oculi. In addition, the landmark of three density points was

identified in relation to the muscular entrance of the facial nerve of temporal and zygomatic branches (39, 40 and 42mm for the upper, middle, and lower points, respectively).

Understanding the innervation of the temporal region is critical to avoiding local (i.e., temporal) and distant (e.g., forehead, peri-orbital, lower face) complications following filler injection. Damage to the TFN can be caused by compression, traction (pull) or transection. Directing the forces towards the bone rather than the fascia during subperiosteal dissection may be employed to reduce the risk of injury to the nerve. The facial nerve, however, is still at risk of traction and/or compression injury, but primarily when the fasciae is being elevated off the bone of the zygomatic arch and the orbital rim. This risk, often associated with surgical procedures, is reduced by careful elevation of the fascial-pericranial flap; To prevent its injury, pulling on the fascial-pericranial flap with fishhooks should be avoided. A fat pad exists between two layers of deep temporal fascia that is nearly avascular in nature, offering a safe zone with negligible risk to the frontotemporal branch of the TFN.[59] In addition, the disposition of the ramus frontalis can be used to help guide submuscular and subfascial procedures and prevent injury as it runs parallel and just caudal to the frontal branch of the STA.[60] The frontal branch of the STA may also serve as a landmark for such procedures as the frontalis branch of the TFN risks injury inferior to this level.

Ligaments and fat compartments

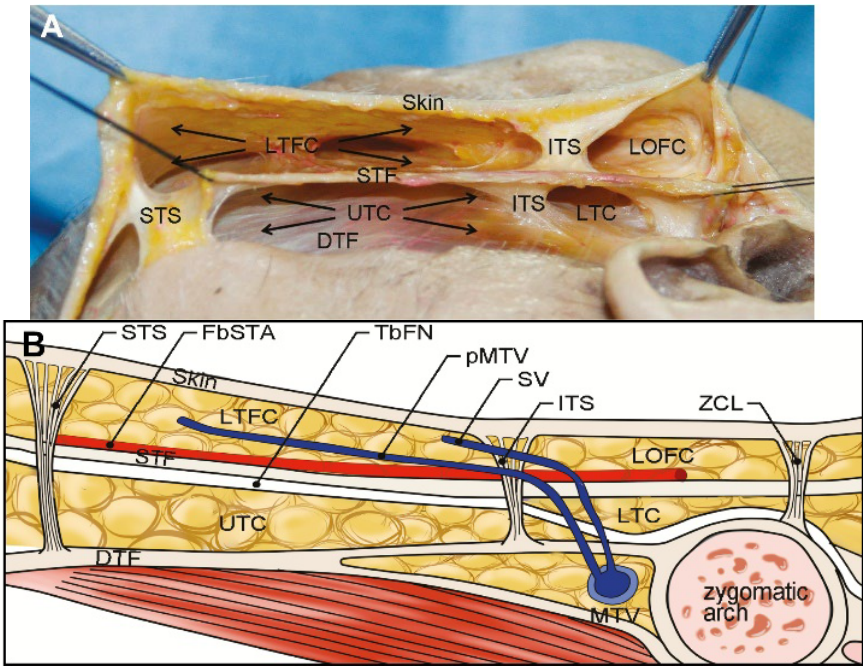
In the temporal region, a series of ligamentous structures can be identified that run perpendicular to the temporal fasciae.[62] Retaining ligaments of the temporal region include the superior and inferior temporal septa, the orbicularis retaining ligament and the zygomatic cutaneous ligament. The inferior temporal septum divides the subcutaneous fatty layer into the lateral temporal fat compartment and the lateral orbital fat compartment. In addition, its divides the areolar tissue into upper and lower compartments.[63] A number of ligamentous structures have been identified perpendicular to the temporal fasciae and found to contribute to the formation of separate divisions within the temporal region.[62] The superior temporal septum (STS) is positioned along the superior temporal line of the skull, originating from the periosteum where it transitions to deep temporal fascia. The inferior temporal septum (ITS) instead is formed by the fusion of superficial temporal fascia and deep temporal fascia, extending horizontally from the lateral corner of the temporal ligamentous adhesion towards the superior crus of the helix. Additionally, the orbicularis retaining ligament (ORL) was found to encircle the orbit as it arises from the periosteum of the orbital rim and crosses the orbicularis oculi muscle where it enters the skin and lid-cheek junction. Lastly, the zygomatic cutaneous ligaments (ZCL) are comprised of adhesions at the level of the lower zygoma and positioned inferior to the zygomatic arch.

The distribution of fat compartments and the characteristic of neurovascular structures in temporal region have been previously described. In a total of ten temples among the eight cadavers, a thin layer of fat tissue was found in the layer of the loose areolar tissue, and at the level of the superior orbital margin, the deep temporal fascia

split into deep and superficial layers encompassing the superficial temporal fat pad.[62] The position of the ITS separates the subcutaneous fat tissue layer into two compartments: (1) the lateral temporal cheek fat compartment (LTFC) and (2) the lateral orbital fat compartment (LOFC) (Figures 16, 17). The ITS also creates two deep septum compartments within the loose areolar tissue layer, being the upper temporal compartment (UTC) and the lower temporal compartment (LTC) (Figures 16, 17). In total, four separated temporal fat compartments were identified as ideal receipts for temporal hollowing procedures.

Figure 16

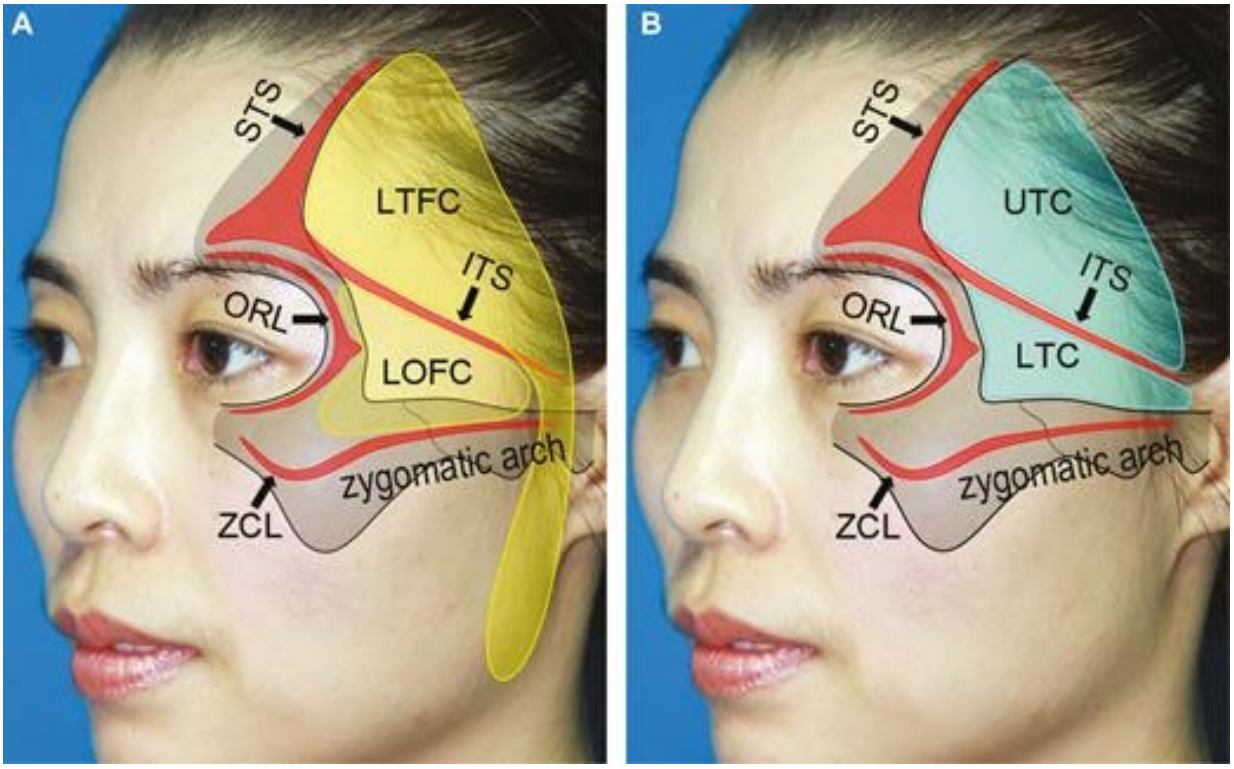
Separated Compartments in the Temporal Region



Note: (A) The ligamentous and compartmental structures in the temporal region as demonstrated on a 64-year-old female cadaver. (B) Illustration demonstrating the ligamentous, compartmental, and neurovascular structures in the temporal region. In the temporal region, the three vertical ligamentous structures divide the two horizontal tissue layers into four separated compartments. The LTFC and LOFC are located at the subcutaneous tissue layer; the UTC and LTC are located at the loose areolar tissue layer. LTFC = Lateral temporal-cheek fat compartment; LOFC = Lateral orbital fat compartment; UTC = Upper temporal compartment; LTC = Lower temporal compartment; STS = Superior temporal septum; ITS = Inferior temporal septum; ORL = Orbital retaining ligament; ZCL = Zygomatic cutaneous ligament. From "Anatomical Study of Temporal Fat Compartments and its Clinical Application for Temporal Fat Grafting," by Huang, Hie, Wang et al., 2017, Aesthetic Surgery Journal, 37(8), 855-862 (https://doi:10.1093/asj/sjw257).[62]

Figure 17

Surface Projection of Fat Compartments and Septum Compartments in the Temporal Region



Note: Surface projection of fat compartments (A) and septum compartments (B) in the temporal region as demonstrated on a 37-year-old female patient. LTFC = Lateral temporal-cheek fat compartment; LOFC = Lateral orbital fat compartment; UTC = Upper temporal compartment; LTC = Lower temporal compartment; STS = Superior temporal septum; ITS = Inferior temporal septum; ORL = Orbital retaining ligament; ZC = Zygomatic cutaneous ligament. From "Anatomical Study of Temporal Fat Compartments and its Clinical Application for Temporal Fat Grafting," by Huang, Hie, Wang et al., 2017, Aesthetic Surgery Journal, 37(8), 855-862 (https://doi:10.1093/asj/sjw257).[62]

The aging temporal fossa

With age, a loss of fullness and roundness of the facial contours transforms the face. Loss of volume culminates from thinning of epidermis, a loss of skin elasticity, atrophy of muscle and subcutaneous fat, and bony changes.[64,65] Facial structures begin to gradually weaken in the third decade with noticeable changes in appearance.[41] On

average, epidermal thickness decreases nearly 6.4% per decade along with a reduction in epidermal cell abundance, occurring particularly in women and in specific anatomical regions (e.g., face, neck, upper chest, extensor surface of hands and forearms).[64] Similarly, the dermal layer of the skin loses molecular integrity with age, characterized as a decrease in dermal thickness, number of mast cells and fibroblasts and reduction in collagen and elastin activity. As a result of reduced interdigitation and loss of dermal papillae, the dermal-epidermal junction flattens and increases skin fragility. These structural and functional changes further lead to wrinkle formation and diminished skin elasticity in aged individuals. Soft tissue (subcutaneous fat, muscle and fascia) are also impacted by the aging process.[66] A decline in subcutaneous fullness of the forehead reveals the muscles of facial expression, resulting in the appearance of wrinkles or folds. Age-related loss of facial volume occurs across tissue planes, from the bone to the epidermis.[67] In the subdermal soft tissues of the face, volume loss is characterized by depletion of the superficial and deep fat compartments.[68] Fat atrophy and redistribution of fat deposits change the shape of the face and accentuate the aging process, causing depressions in the orbital, temporal and buccal spaces.[65] The shape of the face is transformed from an “upside-down egg” to a “peanut,” the latter shape associated with an imbalanced, aged appearance.[69,70]

Atrophy of the temporal muscle and temporal fat pad significantly contribute to the appearance of temporal hollowing.[70] Temporal hollowing is a process that exposes the boniness of the skull, resulting in a sunken or “skeletal” look. Temporal hollowing narrows the upper third of the face, thus unbalancing the facial proportions. Furthermore, loss of temporal support to the lateral brow, combined with loss of fullness in the upper eyelid,

may create the impression of brow ptosis; a condition where the eyebrow descends to or below the superior orbital rim.[71] These age-related structural changes to the temporal fossa affect both anterior and lateral profile views and are not concealed with the application of topical camouflaging agents, such as makeup.

Temporal hollowing has been described as the result of increased concavity of the bones surrounding the temporal fossa (temporal, parietal, sphenoid, and frontal bones of the skull).[6] However, the results of one anatomic survey of forty-nine young skulls (aged 18-30 years) and forty-nine senescent skulls (aged over 69 years) suggested that the bony anatomy of the temporal fossa is stable throughout age and does not contribute to hollowing.[72] Instead, the authors suggested that the concavity of the temporal bones becomes more apparent as the temporalis muscle and temporal fat pad recede to reveal the zygomatic arch and temporal fusion line.[65,66] Subsequent work by Cotofana et al[73,74] confirmed age-related bony changes in the cranium, in a sample of 157 subjects (ten males and females in the following age groups: 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80-89 years, and eight males and nine females between 90-98 years of age) using CT multiplanar scan comparisons.[73,74] The sagittal diameter of the cranium was shown to decrease in males only, while transverse diameter increased in both males and females (significantly only in males). Amounting to a lateral expansion of the skull, these changes could accentuate the lateral orbital rims, temporal crests, and zygomatic arches. This augmentation of the bony prominences of the lateral aspects of the skull could contribute to the appearance of a skeletonized face in older people. Further, the volume of the calvaria decreased in both genders with age (i.e., loss of 5.1% in females and 5.4% in males), which contributes to age-related tissue laxity

(Cotofana, Gotkin, Ascher et al., 2018).[74] To assess whether there is a difference between the anatomy of the temporal fossa of males and females, the current author and his associative team performed a cross-sectional CT-imaging study. If differences based on gender and age occur, the position of vessels within the fossa may vary by group. The study background, methodology and findings are presented in the following section.

Project A- Gender effects of temporal hollowing

The objective of this study was to investigate the various parameters of the temporal region and to relate them to clinically relevant observations, with the hopes of providing numeric support for clinical applications that ultimately increase patient safety and the aesthetic outcome during temporal volumizing procedures. The study relied on retrospectively analysed cranial computed tomographic (CT) images of fifty-eight previously scanned consecutive patients. The indications for the cranial CT scans were cerebrovascular incidents or other clinical issues related to the neural tissue of the head and neck, i.e., brain and cervical spinal cord. Patients were excluded from this study if their temporal skin surface or the anatomy of their temporal region was affected by trauma or tumours, or any other clinical condition that could have disrupted the integrity of their temporal anatomy; this was verified by the screening process before transferring the data for further analyses. Their datasets were stored in the radiology database of the Research and Practical Clinical Centre for Diagnostics and Telemedicine Technologies of the Moscow Health Care Department, Moscow, Russia, and sampled for the purposes of this study. The ethics committee of the Department of Health, Moscow, Russia approved the study (retrospective analysis of CT scans; protocol number 5). Before the initial cranial

CT scan, patients gave their informed consent for the use of their demographic and CT imaging data for research and educational purposes. The analyses of their cranial CT-scans occurred between January and March 2020.

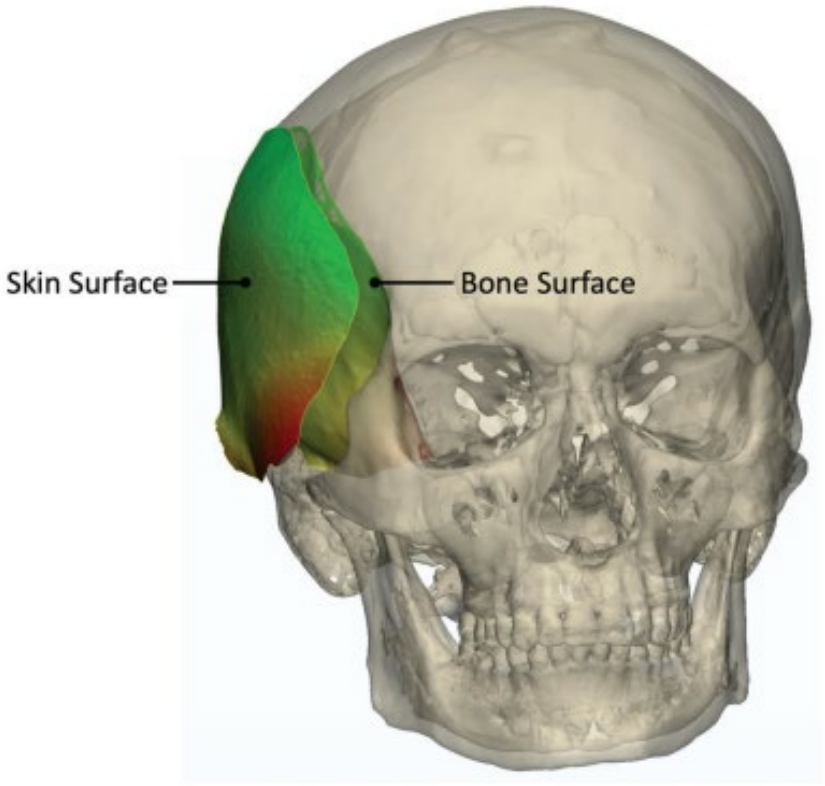
CT scans were acquisitioned via a Toshiba Aquilion 64 slice scanner (Toshiba Medical Systems Corporation, Ōtawara, Tochigi, Japan) with the following scanning parameters: voltage 120 kV, slice thickness 0.47 mm, field of view 220 mm and tube current 140 mA. CT scans were imported from the radiologic database into the Mimics Innovation Suite software (Materialise NV, Leuven, Belgium) and the temporal region was bilaterally analyzed. The boundaries of the temporal fossa were as follows:

- Anterior – the posterior surface of the frontal process of the zygomatic bone
- Posterior – a vertical line perpendicular to Frankfort plane passing through the anterior margin of the external acoustic meatus connecting to the temporal crest
- Superior – the temporal crest
- Inferior, for bone – the infratemporal crest
- Inferior, for skin – the upper margin of zygomatic arch (Figures 18, 19, 20).

The surface of the skin and the surface of the bones forming the base or foundation of the temporal fossa were identified by the software algorithm due to differences in Hounsfield units on the CT scans (Figure 18). Distance measurements (minimum and maximum distance) between the two surfaces were automatically calculated and the volume between these two surfaces was computed; the latter was regarded as the soft tissue volume of the temporal fossa (Figure 19). All measurements were based on the Hausdorff minimal distance algorithm (Figure 20).[75]

Figure 18

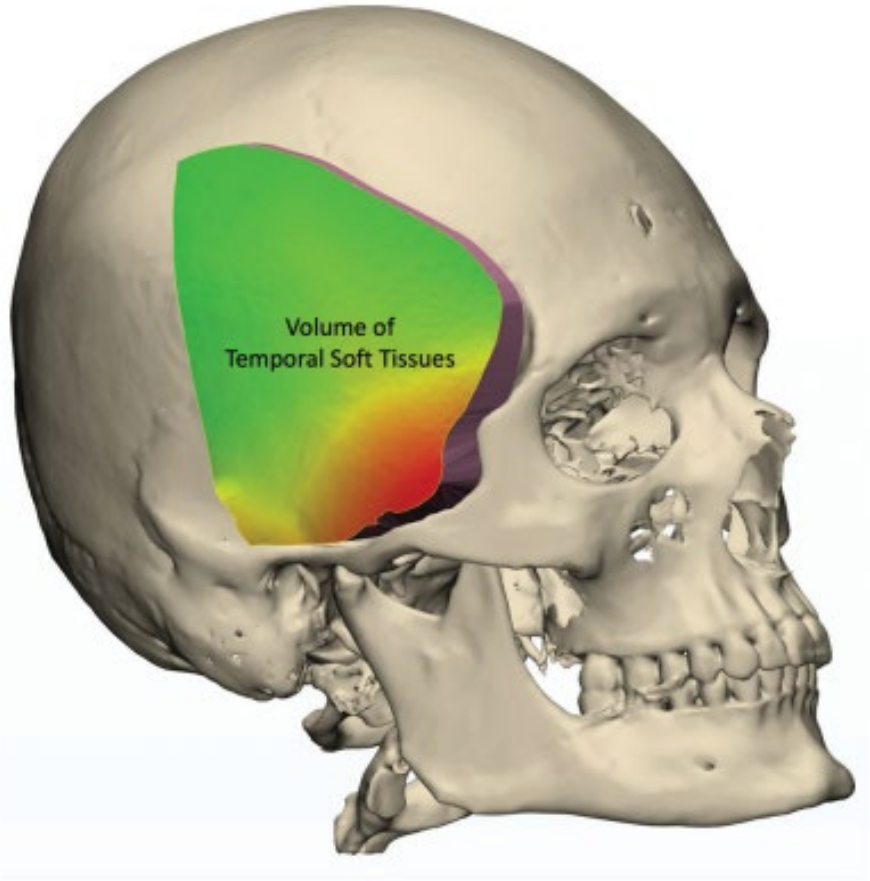
Three-Dimensional Reconstruction of a Cranial CT Image With the Skin and the Bone Surface Highlighted



Note. The margin of the temporal bony surface is the posterior surface of the frontal process of the zygomatic bone (anterior), the temporal crest (superior), infratemporal crest (for bone, inferior), upper margin of zygomatic arch (for skin, inferior), and a vertical line passing through the anterior margin of the external acoustic meatus connecting to the temporal crest. The skin surface is adjusted to these boundaries. From "Differences in Temporal Volume between Males and Females and the Influence of Age and BMI? – A Cross-Sectional CT-Imaging Study," by Nikolis, Frank, Guryanov et al., 2021, *Facial Plastic Surgery, 37*(5), 632-638 (https://doi:10.1055/s-0041-1725201).[9]

Figure 19

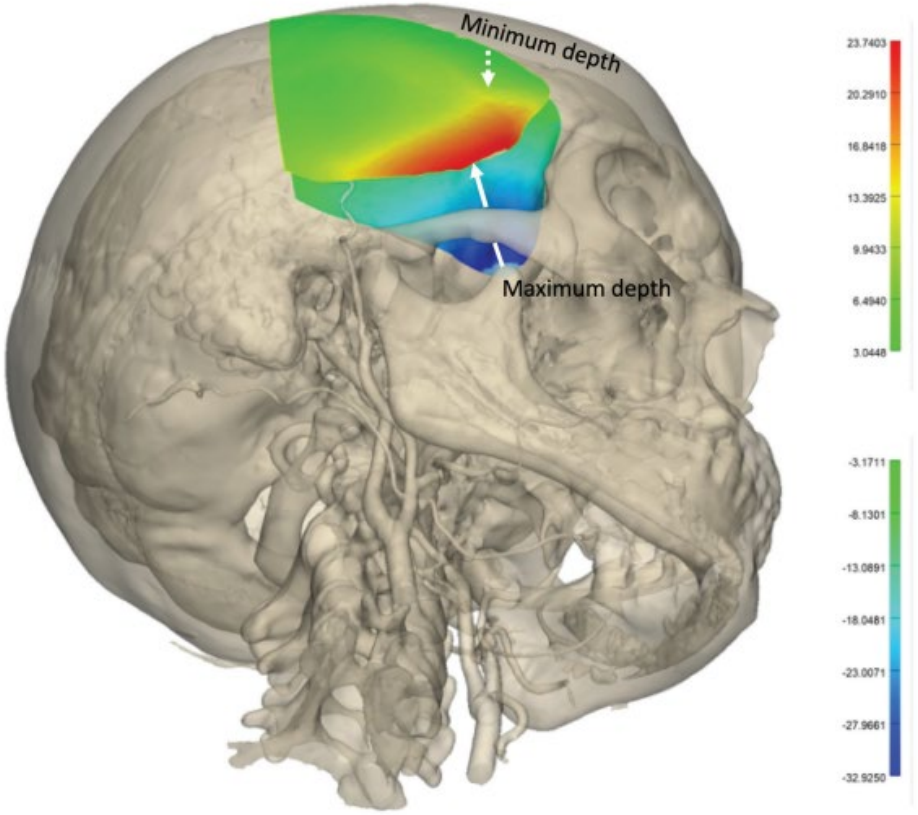
Three-Dimensional Reconstruction of a Cranial CT Image Showing the Volume of the Temporal Soft Tissues Located Between the Skin and Bone Surfaces



Note. The depth of the temporal fossa is colour coded with red areas indicating greatest depth. From “Differences in Temporal Volume between Males and Females and the Influence of Age and BMI? – A Cross-Sectional CT-Imaging Study,” by Nikolis, Frank, Guryanov et al., 2021, *Facial Plastic Surgery, 37*(5), 632-638 (https://doi:10.1055/s-0041-1725201).[9]

Figure 20

Three-Dimensional Reconstruction of a Cranial CT Image Exemplifying the Measuring Methods According to the Hausdorff Method



Note. For each pixel in the skin surface and for each pixel in the bone surface, the smallest distance between them was computed. The smallest depth of the temporal fossa was measured as the distance from skin surface to bone surface (white arrow oriented superficial to deep), whereas the maximal depth of the temporal fossa was measured as the distance from bone surface to skin surface (white arrow oriented deep to superficial). From “Differences in Temporal Volume between Males and Females and the Influence of Age and BMI? – A Cross-Sectional CT-Imaging Study,” by Nikolis, Frank, Guryanov et al., 2021, *Facial Plastic Surgery, 37*(5), 632-638 (https://doi:10.1055/s-0041-1725201).[9]

The Hausdorff algorithm determines the smallest distance between pixels of two marked surfaces: the skin and the bone surface and each surface had more than 1000 pixels. This method allows measurement of precise distances between uneven and not parallel surfaces and, furthermore, to determine the volume between them.[76] Comparable to previous applications,[75,77-79] the Hausdorff algorithm was applied to the temporal fossa – known to have varying surfaces both on bone and on the skin surface.

Testing for homogeneity and normal distribution revealed non-normally distributed data. This resulted in the decision to conduct non-parametric statistical testing (Shapiro-Wilk test with $p < 0.05$) and to report values as median and the respective interquartile range. No statistically significant differences between facial sides were identified in any of the tested parameters with all $p \geq 0.250$. This enabled the fusion of parameters of the left and right temple (each $n = 58$) and the subsequent calculations using a sample size of $n = 116$ temples. According to a recent publication, the mean age for menopause in the western civilization was determined to be 50 – 51 years.[80] This cut-off value was used in the statistical analyses to determine pre-menopausal from post-menopausal females, i.e. females below the age of 50 vs. females above the age of 51 years. Bivariate correlations computing Spearman's correlation coefficient (r_s) were run to identify linear relationships. Influence of age, gender and BMI were identified using generalized linear models. Differences in results were considered statistically significant if $p \leq 0.05$. All tests were run using SPSS Statistics 23 (IBM, Armonk, NY, USA).

The evaluated sample consisted of twenty-eight male and thirty female Russian Caucasian individuals with a median age of 53 years and an interquartile range of 34 years [total data range: 22.0 – 80.0] and a median body mass index (BMI) of 27.00 kg/m^2

and an interquartile range of 6.94 kg/m^2 [total data range: 18.0 – 43.5]. The median age of the female study participants was 51.5 (33) years whereas the median BMI was 25.94 (7.26) kg/m^2. The median age of the male study participants was 54.5 (36) years whereas the median BMI was 27.31 (5.90) kg/m^2. No statistically significant difference between genders for age ($p = 0.901$) or BMI ($p = 0.269$) was detected.

Overall, the location of the maximum depth of the temporal fossa was found to be inferior and anterior, whereas the minimum depth was found along and in proximity to the temporal crest (Figures 18, 19, 20). The maximum depth (maximal distance between skin surface and bone surface) was 32.76 (5.76) mm in males whereas in females it was 29.90 (4.87) mm with $p = 0.004$. The minimum depth (minimum distance between skin surface and bone surface) was 3.78 (1.17) mm in males whereas in females it was 3.07 (1.05) mm with $p < 0.001$.

Adjusted generalized linear models (age, gender, and BMI) revealed that an increase in one unit of BMI resulted in an increase of 0.42 mm in the distance between skin surface and bone surface ($p < 0.001$). Age- and BMI-matched males had, on average, a greater maximal temporal depth by 1.58 mm compared to females ($p = 0.008$). Interestingly, there was no statistically significant influence of age on the maximal depth, with $p = 0.517$.

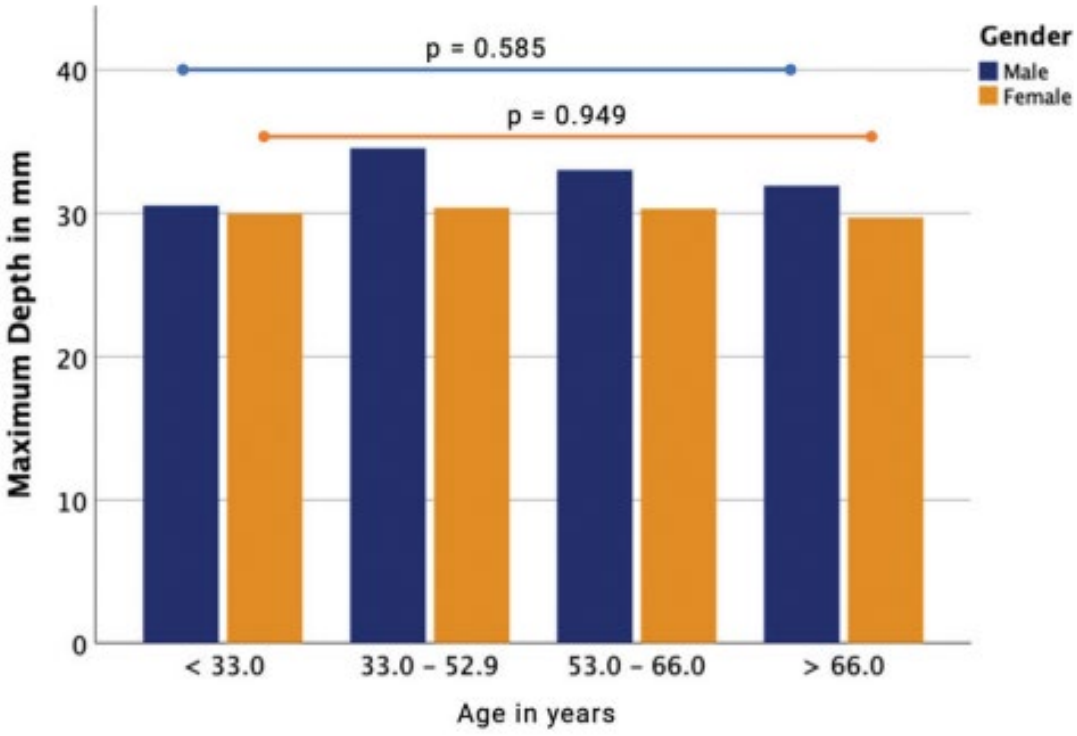
The median skin surface area in males was 5100.5 (708) mm^2 whereas in females it was 4208.5 (893) mm^2 with $p < 0.001$. Adjusted generalized linear models (age, gender, and BMI) revealed that an increase in age by one year resulted in a decrease of temporal skin surface area of 10.3 mm^2 ($p = 0.001$) and that an increase in one unit of BMI resulted in an increase of 33.2 mm^2 ($p = 0.016$) in temporal skin surface area. Males had on

average 750.0 mm^2 larger temporal skin surface area compared to age and BMI-matched females with $p < 0.001$.

The median bone surface area in males was 5329 (690) mm^2 whereas in females it was 4477 (888) mm^2 with $p < 0.001$. Adjusted generalized linear models (age, gender) revealed that an increase in age by one year resulted in a decrease of temporal bone surface area of 9.7 mm^2 ($p = 0.006$) and that males had, on average, 692.6 mm^2 larger temporal bone surface area compared to age-matched females.

The median temporal soft tissue volume was 55.10 (17.89) cc in males whereas in females it was 41.27 (9.51) cc with $p < 0.001$. An increase in BMI correlated with a statistically significant increase in volume in both males ($r_s = 0.441$, $p = 0.001$) and females ($r_s = 0.414$, $p = 0.001$). However, an increase in age correlated with a statistically significant decrease in volume only in females ($r_s = - 0.397$, $p = 0.002$), not in males ($r_s = 0.036$, $p = 0.791$). Adjusted generalized linear models (age, gender, and BMI) revealed that an increase in age by one year resulted in a decrease of temporal soft tissue volume of 0.17cc ($p = 0.013$) and that an increase in one unit of BMI resulted in an increase of 1.12cc ($p < 0.001$) volume. On average, males had 11.04cc greater temporal soft tissue volume compared to age and BMI-matched females with $p < 0.001$. Comparing the volume between pre-menopausal (< 50 years) and post-menopausal females (> 51 years), the median temporal soft tissue volume was 46.63cc (11.94) vs. 40.32 cc (5.69) with $p = 0.014$; this trend was not observed in males using the same stratified statistic testing ($p = 0.831$) (Figure 21).

Figure 21
Differences in the Median Temporal Soft Tissue Volume



Note: Bar graph with the respective 95% confidence interval (CI) showing differences in the median temporal soft tissue volume between males and females of age below 51 years and age above 51 years. From "Differences in Temporal Volume between Males and Females and the Influence of Age and BMI? – A Cross-Sectional CT-Imaging Study," by Nikolis, Frank, Guryanov et al., 2021, *Facial Plastic Surgery, 37*(5), 632-638 (https://doi:10.1055/s-0041-1725201).[9]

The results of this cross-sectional CT imaging-based study confirm clinical and anatomic observations: the temporal fossa is deepest close to the lateral orbital rim where it fuses with the zygomatic arch. However, accurate numerical data were not available previously and the current study closes this knowledge gap. The maximum depth in males was 32.76 mm whereas in females it was 29.90 mm; this represents a statistically significant difference of $p = 0.004$. The measurements performed were based on the Hausdorff method; this calculates the distance between two surfaces independent of their shape. Utilizing this mathematical algorithm is novel and provides a unique opportunity to conduct precise estimates of the depth of the temporal fossa despite none of the surfaces (i.e., skin surface, bone surface) being linear in shape. These results indicate that if minimally invasive soft tissue filler volume augmentation of the temporal fossa is planned utilizing the deep, supraperiosteal injection technique,[81] the needle length should be selected appropriately. In males, a longer needle should be selected, compared to females, to establish bone contact and to allow for supraperiosteal product placement.

The results of this study also revealed that the area in proximity to the temporal crest had the smallest distance between skin surface and bone surface with 3.78mm in males and 3.07mm in females ($p < 0.001$). These findings imply that the depth of the temporal fossa becomes shallower in its cranial aspects with thinner, soft tissues covering the bone closer to the temporal crest. This, in and of itself, highlights the risk of penetrating the integrity of vessels varies with age as the bony vault changes and location of vessels. It can be hypothesized that the administration of volumizers in more cranial locations of the temporal fossa might result in better surface projection due to the reduced soft tissue cover; this might affect a better restoration of temporal volume per unit volume of product

administered.[82] This effect was recently investigated in a clinical interventional study; the authors reported that the deep, supraperiosteal (needle) injection technique in the anterior temple needed 69% more soft tissue filler to achieve a non-different aesthetic outcome when compared to a subdermal (cannula) injection technique positioned in the same location.[83] The results of that study can be explained by the reduced thickness of soft tissue covering the administered product. This supports more cranially located product administration wherein a smaller temporal soft tissue thickness is present. Furthermore, a previous study reported on the safety aspects of the supra-periosteal injection in the superior temple (as opposed to the inferior temple); this could favour a more superior dermal access point to perform minimally invasive temporal volumizing procedures in the future.[50]

The anterior and inferior location within the temple was identified to be the deepest location of the temple; this can be related to the underlying anatomy – unique and not observed in more cranial locations of the temple. The following layers can be identified here: skin, superficial fatty layer, superficial temporal fascia, deep fat (containing the frontal branches of the facial nerve), superficial lamina of the deep temporal fascia, superficial temporal fat pad (enclosing the middle temporal vein), deep lamina of the deep temporal fascia, temporal extension of the buccal fat pad, temporalis muscle and periosteum.[4] The presence of these many layers in the inferior (anterior and posterior) temple predisposes for age, BMI and gender related differences in temporal soft tissue volume and this is confirmed clinically: the location where temporal hollowing is most frequently observed is the anterior and inferior temple. The loss in volume in this location additionally accentuates the visibility of adjacent bony prominences, i.e., the temporal

crest, the lateral orbital rim, and the upper margin of the zygomatic arch. This promotes an “aged,” skeletonized facial appearance. Volume loss of the inferior posterior temple is of less clinical relevance (despite having the same layered anatomy) due to the coverage with hair.

The results of the present study revealed that males had a larger temporal soft tissue volume compared to females – 55.10 cc vs. 41.27 cc, respectively – and this difference was statistically significant with $p < 0.001$. This could be due to the greater bone surface area and the greater skin surface area measured – the results of gender-related anthropometric differences confirmed in previous CT imaging studies.[73,74,84] Interestingly, an increase in one unit of BMI resulted in an increase of 1.12cc ($p < 0.001$) of temporal soft tissue volume and this was reflected in similar correlation coefficients in both genders: males $r_s = 0.441$, $p = 0.001$ and females $r_s = 0.414$, $p = 0.001$. This indicates that an increase in BMI is reflected in an increase in temporal soft tissue volume independent of gender; this is plausible due to the presence of multiple fatty layers and fat pads of the temple. However, the influence of age on temporal soft tissue volume manifested differently in males and females. In males, no statistically significant correlation was found between age and volume ($r_s = 0.036$, $p = 0.791$) whereas in females, an inverse correlation was found ($r_s = - 0.397$, $p = 0.002$). Based on the sample investigated in this study, at greater age, the temporal soft tissue volume was reduced in females but not in males. Further statistical analyses, with stratification for gender, revealed additional differences between pre-menopausal and post-menopausal women. Women under 50 years of age have a larger temporal soft tissue volume compared to those women over 51: 46.63 cc vs. 40.32 cc, respectively, with $p = 0.014$. When

conducting the same statistical testing in males, no such difference was found when using the same age cut-off values (below 50 years vs. above 51 years) with p = 0.831. This lends to the concept that female patients require further measures to prevent vascular AEs, given their distinct and unique anatomic changes.

In our cross-sectional study, these results indicate that females at a greater age than the average age for menopause have a statistically significant reduction in temporal soft tissue volume. This would likely influence this patient population to seek temporal augmentation procedures.[85] The demand for these procedures is based on the natural course of facial aging and on the process of sarcopenia – the loss of muscle mass. The latter is most likely related to the post-menopausal hormonal status of these women.[80,86-89] Sarcopenia is associated with loss in muscle mass (among other things) and would explain the effects observed in our sample of sixty female temples: a reduction in temporal soft tissue volume due to a reduction in temporalis muscle volume and temporal fat atrophy. In males, this effect was not observed despite equal statistical testing and similar sample size; this would support the hypothesis as males are not affected by this hormonal change when using the same statistical cut-off value for age.

A limitation of the study is that all the individuals studied were from a distinct geographical region and all were Caucasian; results might differ if analyses were conducted on other ethnicities. Another limitation of the study is that analyses are based on a cross-sectional data set and any changes detected are found based on the evaluation of younger vs. older individuals, not the same person studied over time. Cause and effect relationships and conclusions are thus to be considered with caution. A stronger study design would be the longitudinal follow-up of the same individuals at

different time points, however these types of studies are subject to larger drop-out rates and biased if the assessment technology changes between baseline and follow-up – for instance, if another CT-scanner was used to record the follow-up images due to technologic advancements. Regardless, the important findings in the study should caution the injector that different groups of patients have different risk factors for arterial injury and consequent embolization of product.

The results of this cross-sectional CT-imaging study confirmed previous clinical and anatomical observations and added numerical evidence to those observations for a better clinical integration of the data. The volume of the temporal fossa differs between genders with males having a greater temporal volume compared to females. Increases in BMI resulted in an increase in volume; this can be explained by the presence of the various fatty layers and fat pads of the temple. This surely will change the position of the superior and deep temporal vessels. Advanced age, however, decreased the temporal soft tissue volume in females and this effect was more dominant in post-menopausal females. This age-related effect was interestingly not observed in males when conducting the same statistical approach.

Scales for measuring temporal hollowing

Several scales have been developed to measure the degree of subject temporal hollowing and have been used to validate the efficacy of treatments investigated in clinical trials. For example, the Hollowness Severity Rating Scale (HSRS) is a 4-point scale that grades temporal depression from a score of 1 (absent) to 4 (severe). The HSRS provides a detailed description of each grade and corresponding expectations for post-treatment

improvement (e.g., excellent correction expected from injectable implant; Figure 22). Several clinical trials have employed the HSRS to evaluate treatment of temporal rejuvenation. One study demonstrated clinical efficacy and safety of small gel particle HA (SGP-HA) for temple augmentation, by evaluating physician-assessed improvement in HSRS ratings from baseline to follow-up visits over the course of twelve months.[90] Another study utilized the HSRS to analyze the safety and efficacy of a targeted fat-grafting procedure for temporal hollowing augmentation.[91] Pre- and post-operative assessments using the HSRS were conducted, and results demonstrated an overall improved clinical appearance, with 74% of patients having at least a two-point change on the HSRS following the procedure. Studies evaluating the use of autologous fat grafting for volumizing the temporal region have also used the HSRS to quantify improvement following treatment.[92,93] While the HSRS has been used as an assessment tool in different clinical settings, it has not been validated; a concern previously emphasized by Carruthers et al.[94] Therefore, further studies are needed to assess the reliability and sensitivity of the HSRS. Another limitation of the HSRS is that it is only descriptive in nature and lacks corresponding imagery depicting the various grades.

Figure 22
Hollowness Severity Rating Scale

Score	Description
4	Severe: very hollow temples. Significant improvement is expected from injectable implant.
3	Moderate: moderately hollow temples. Excellent correction is expected from injectable implant.
2	Mild: shallow hollow temples; minor facial feature. Implant is expected to produce a slight improvement in appearance.
1	Absent: no hollowness.

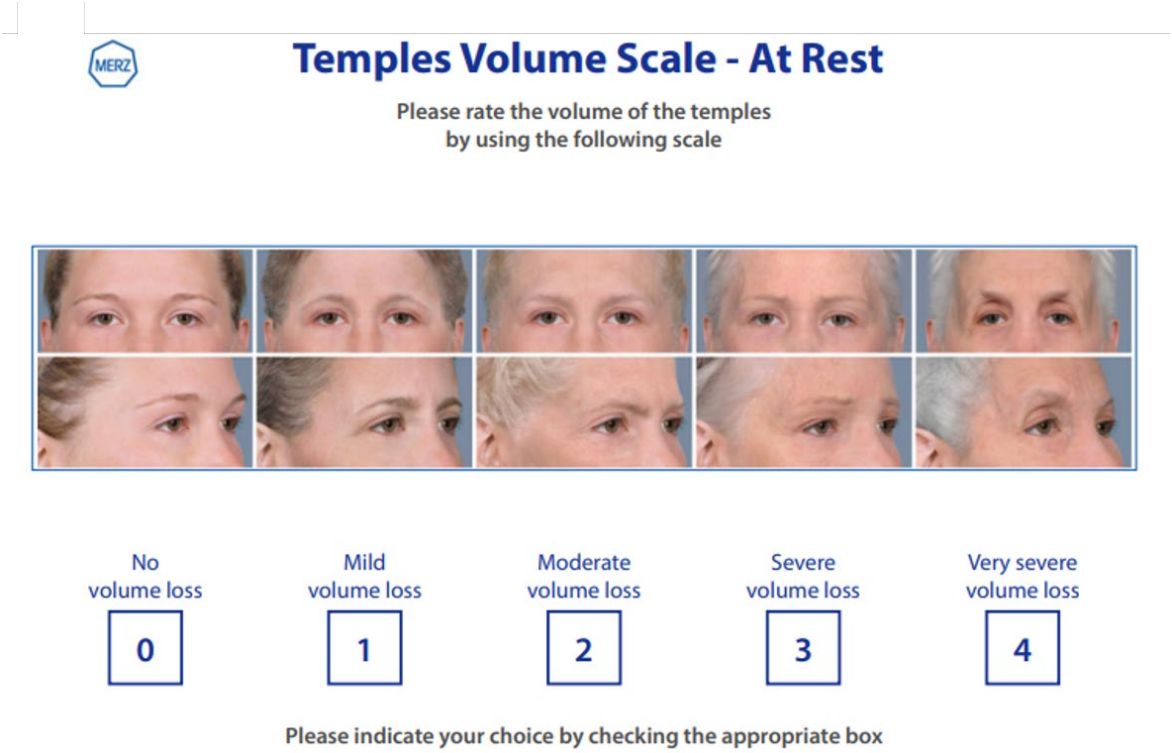
Note: Amended from "A 12-Month, Prospective, Evaluator-Blinded Study of Small Gel Particle Hyaluronic Acid Filler in the Correction of Temporal Fossa Volume Loss," by A. Moradi, A. Shirazi and J. Moradi, 2013, *Journal of Drugs in Dermatology, 12*(4), 470-475.[90]

Nonetheless, validated photonumeric scales are available. The Merz Temple Volume Scale (MTVS) is one such example. The MTVS is a five-point photonumeric scale used to rate the appearance of the temporal fossa and grade severity of volume loss. The scale ranges from 0 (no volume loss) to 4 (very severe volume loss). The MTVS has been used in clinical trials as a means of evaluating correction of volume loss following treatment with injectables. Juhász et al[95] examined the safety and efficacy of calcium hydroxylapatite with integral lidocaine [CaHA(+)] to treat temporal hollowing over the course of twelve months. The MTVS was used to determine subject eligibility, with moderate (score of 2) to very severe (score of 4) volume loss as inclusion criteria. The scale was also used to assess temporal volume at baseline and subsequent follow-up visits (day fourteen, week six, and months three, six, nine and twelve). Using the MTVS, investigators concluded that there was an overall improvement in temporal volume resolution following CaHA(+) treatment, with a maximal decrease of two points on the MTVS scale at week six and an overall decrease of one point over the twelve-month study duration. The MTVS ratings were also used to demonstrate significance in temporal volume restoration at every follow-up visit compared to baseline, and further revealed subgroup differences (e.g., gender, skin type, smoking status). More recently, the MTVS was used by Pavicic et al[96] to verify the safety and efficacy of Cohesive Polydensified Matrix (CPM)-HA26 gel, an injectable HA filler, for the treatment of volume deficiency in the temporal region and/or cheeks. MTVS grades of 2 to 4 (i.e., moderate to very severe) were used as inclusion criteria. As a secondary endpoint for clinical effectiveness, investigators evaluated changes in the MTVS (bilateral) from baseline to post-injection follow-up visits (weeks four, twenty-four and forty-eight), along with changes in the Merz

Cheek Fullness Assessment Scale. The photonumeric nature of the MTVS allowed for quantitative analyses and revealed significant temporal volume improvement at all visits following treatment, compared to baseline, with maximal improvement at week four. Although the MTVS has been used to demonstrate clinical efficacy of various injectables for temporal volume correction, a limitation of this scale is the use of a single Caucasian woman to demonstrate severity grades (Figure 23). This lack in subject diversity may lead to difficult interpretations and grading for other patient demographics. The MTVS also fails to include any detailed description of the condition, beyond the categorization of hollowness severity (e.g., mild, moderate, severe).

Figure 23

Merz Validated Temple Scale Assessment



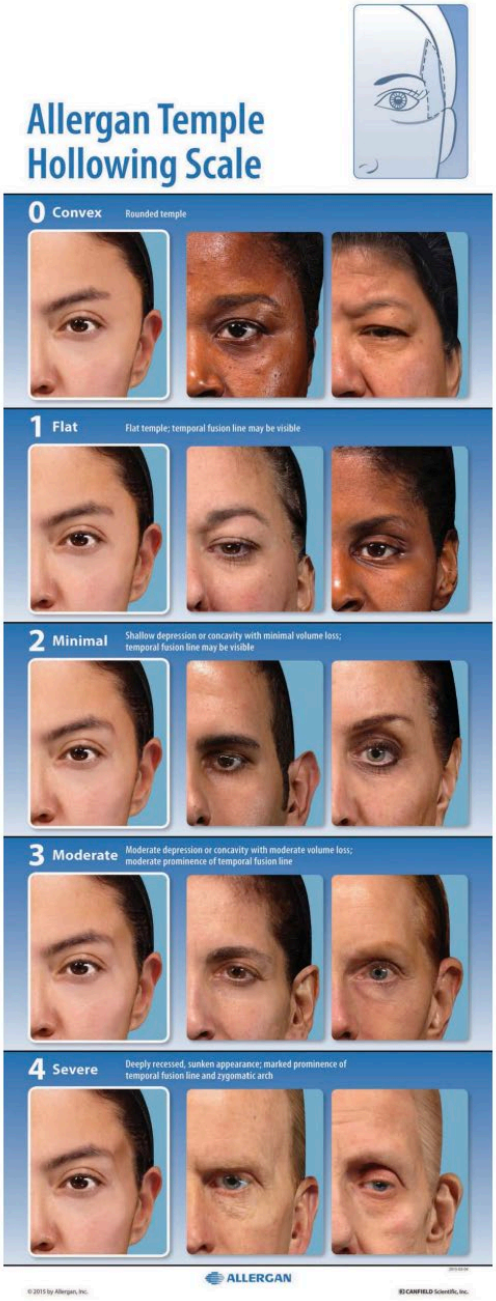
Note: From "Pilot Study Examining the Safety and Efficacy of Calcium Hydroxylapatite Filler With Integral Lidocaine Over a 12-Month Period to Correct Temporal Fossa Volume Loss," by M. L. W. Juhász, M. K. Levin and E. S. Marmur, 2018, *Dermatologic Surgery, 44*(1), 93-100 (https://doi:10.1097/DSS.0000000000001268).[95] Copyright 2014 by Merz Pharmaceuticals, GmbH.

The Allergan Temple Hollowing Scale is another five-point photonumeric scale designed to rate severity of temporal volume deficit. The scale is based on a range from 0 (convex) to 4 (severe) and displays real and morphed images of both men and women with varying Fitzpatrick skin types, for each grade (Figure 24). The scale also features detailed descriptions of each category (e.g., prominence of the temporal fusion line) to help assign the proper rating. An assessment guide for the Allergan Temple Hollowing Scale is also available for additional support on identifying the exact anatomical region under evaluation (Figure 25). The Allergan Temple Hollowing Scale was developed and validated as reported by Carruthers et al,[94] who evaluated the interrater and intrareader reliability of the scale using eight physician raters possessing prior experience with aesthetic photonumeric scales. A total of 291 subjects participated in two live validation sessions wherein the subjects were presented individually to each physician rater for separate evaluations. Results of the study showed almost perfect (mean weighted kappa coefficient = 0.86) interrater and intra-rater agreement, thereby validating the reliability of the Allergan Temple Hollowing Scale. Study findings also confirmed the sensitivity of the scale by demonstrating that a one-point difference between scores corresponds to a clinically significant result. Recently, the Allergan Temple Hollowing Scale was used to evaluate treatment of CaHA(+) for temporal depression.[97] Recruited subjects were required to have a rating of at least 2 (minimal) at baseline and were re-assessed thirty days post-injection. Using the Allergan Temple Hollowing Scale, the physicians observed that all subjects displayed improvement, with nine out of ten subjects achieving a grade 1 (flat) and one subject improving from severe (grade 4) to minimal (grade 2) temporal hollowing. The advantages of the Allergan Temple Hollowing Scale include wide

applicability across genders and races. For example, the authors of the validation study explained that convex temples were defined as the lower limit of the scale, in order to appeal to Asian patients who may prefer a convexly shaped temporal region.[94]

Figure 24

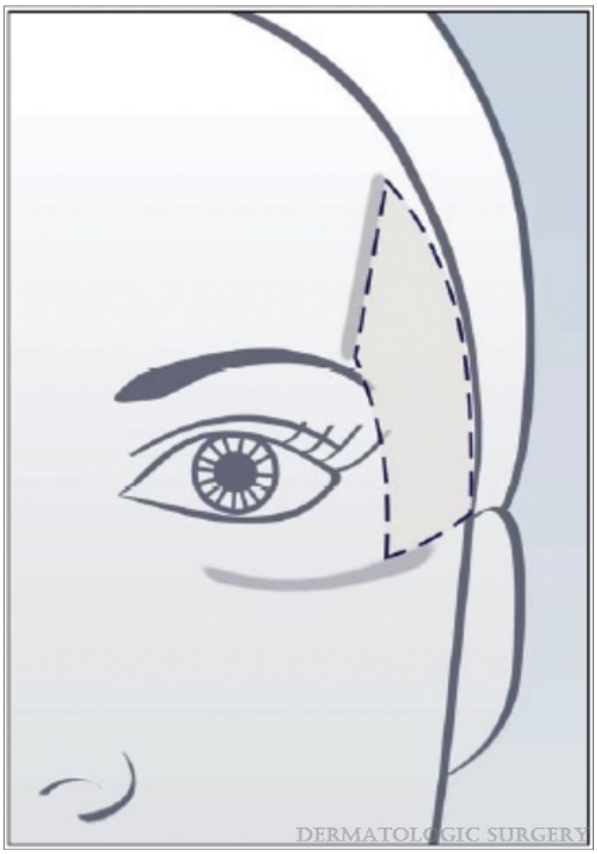
Allergan Temple Hollowing Scale



Note: From "Development and Validation of a Photonumeric Scale for Evaluation of Volume Deficit of the Temple," by Carruthers, Jones, Hardas et al., 2016, *Dermatologic Surgery, 42 Suppl 1*, S203-S210 (https://doi:10.1097/DSS.0000000000000848).[94]

Figure 25

Assessment Guide for the Allergan Temple Hollowing Scale

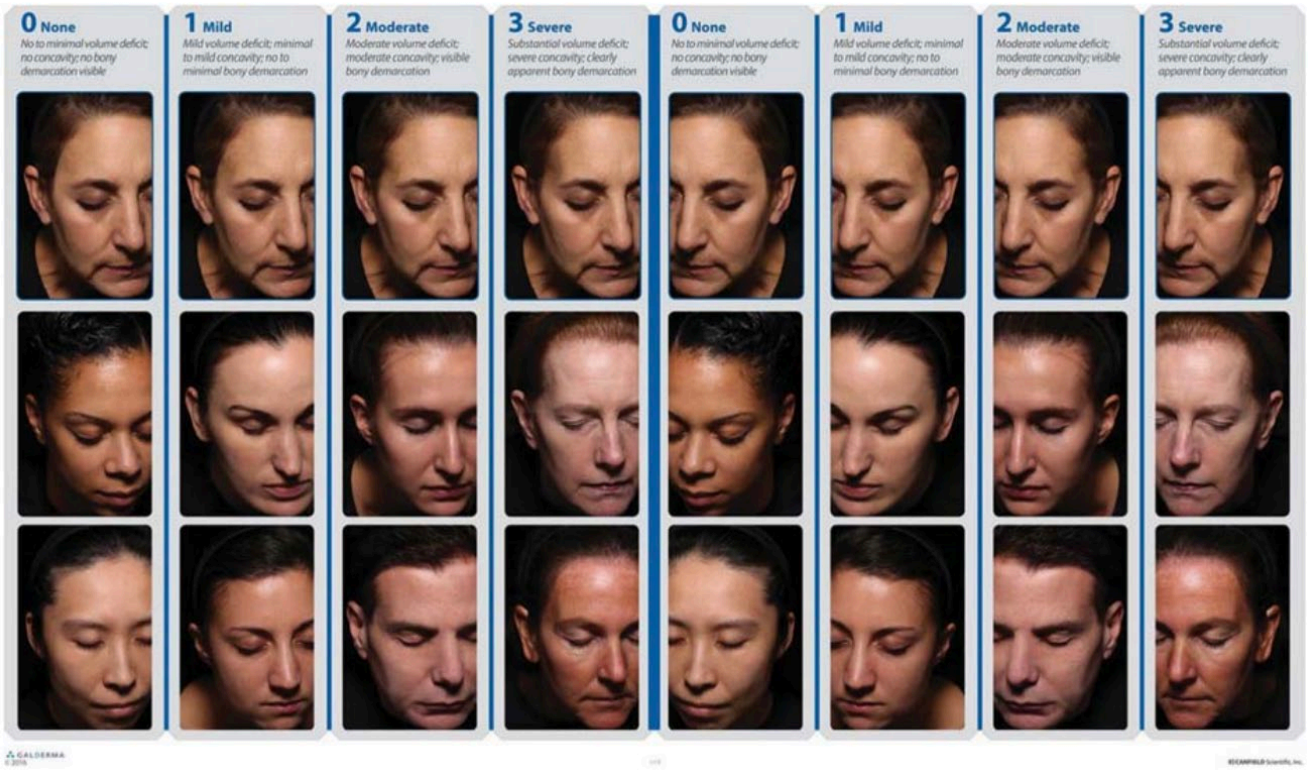


Note: From “Development and Validation of a Photonumeric Scale for Evaluation of Volume Deficit of the Temple,” by Carruthers, Jones, Hardas et al., 2016, *Dermatologic Surgery, 42 Suppl 1*, S203-S210 (https://doi:10.1097/DSS.0000000000000848).[94]

Another photonumeric scale for measuring temporal hollows is the Galderma Temple Volume Deficit Scale (GTVDS). The GTVDS is also inclusive, consisting of images of individuals from varying ages, skin types, and sexes (Figure 26). For grading degree of temporal volume deficit, the four-point scale ranges from 0 (none) to 3 (severe). The GTVDS also includes descriptors of each grade, including severity of concavity and visibility of bony demarcation. A unique feature of the GTVDS is its display of bilateral views of the face, allowing for clear assessment of both temporal hollows. However, the GTVDS is limited by its lack of forward-facing views. Moradi et al[98] recently validated the GTVDS using three evaluators who graded seventy-two subjects on two separate occasions. Sessions were spaced fourteen days apart. Findings revealed substantial intra-observer and interobserver agreement for the GTVDS, with weighted kappa coefficients of 0.74 and 0.72, respectively. Overall exact intra-observer agreement was 70% between the two sessions, while exact interobserver agreement ranged from 68% to 69% between the three evaluators. Therefore, the authors confirmed the validation of the GTVDS as a reliable assessment tool for temporal volume deficit. However, this study did not establish the sensitivity of the scale.[98]

Figure 26

Galderma Temple Volume Deficit Scale



Note: From "Validation of Photonumeric Assessment Scales for Temple Volume Deficit, Infraorbital Hollows, and Chin Retrusion," by A. Moradi, X. Lin, S. Allen, et al., 2020, Dermatologic Surgery, 46(9), 1148-1154.[98]

Treatments for temporal hollowing

Almost a decade ago, authors remarked that temporal hollowing is a significant manifestation of aging that is currently undertreated and predicted that "physicians and patients will come to appreciate the dramatic degree of improvement that can be achieved by restoring volume in the temporal hollow and that this practice will come to be incorporated as a mainstay of overall facial rejuvenation".[99] However, the aesthetic implications of temporal hollowing are still gaining appreciation and this area is still being undertreated.

A recent (2020) review synthesized the available literature on aesthetic temporal augmentation, including currently available methodologies and their accompanying safety and efficacy data.[100] Several treatment approaches were found to exist, including the use of grafts, implants, fillers and flaps.[95,101-107] Each approach was associated with various advantages and disadvantages, and the method ultimately employed was found to be dependent upon patient-specific needs and clinician preference.[100] The following narrative will focus on minimally invasive treatment options for temporal rejuvenation.

Diffuse effects of temporal rejuvenation

The tissues of the face are interdependent, especially the fascial layers, which are connected throughout the face. For this reason, augmentation of the temporal regions may affect other nearby or distant locations. A recent publication (2021) reported two cases where upper eyelid skin tightening was observed after poly-L-lactic acid (PLLA) treatment into the temples.[108] Another study found that the use of a posterior temporal supraperiosteal (supra)-SMAS minimally invasive lifting procedure was shown to treat

temporal hollowing and age-related changes in the mid- and lower face (e.g., marionette lines and jowl deformity).[109] The investigators found that as injection of HA increased the volume of the temporal fat compartment, the skin shifted upwards. Fibrous septae binding the compartment were reoriented, pulling the skin of the mid- and lower face upward and thereby reducing signs of aging.

Permanent dermal fillers

Fat harvested from liposuction of a donor area (e.g., abdomen, thigh, flank) may be transplanted into the face to restore volume and reduce tissue laxity. Fat grafting has a long history, with the first references of its use appearing in literature from the late nineteenth century.[110] However, references to the use of autologous fat for aesthetic correction of the temporal region only appeared in the literature in 2007.[111] After some initial resorption, injections of autologous fat last longer than any known filler, with little-to-no risk of allergic reaction.[52] However, harvesting and transferring autologous fat is associated with greater risk than the use of other commercially available dermal fillers [e.g., hyaluronic acid (HA)].[112-114] The main reason for the increased risk of autologous fat compared to HA dermal fillers is that an embolus formed by HA may be rapidly dissolved with hyaluronidase, which is not an available option for fat.[71]

Semi-permanent dermal fillers

Calcium hydroxylapatite is a dermal filler that stimulates neo-collagenesis and compared to HA, is firmer with a longer duration of effect (i.e., up to eighteen months).[115] A previous open-label pilot study of twenty subjects investigated the use of calcium hydroxylapatite with integrated lidocaine [Radiesse(+)] to correct volume loss in the

temporal fossa. At Baseline, all subjects had moderate to severe temporal fossa volume loss, per the MVTS Assessment ("Merz Temples Volume Scale," 2014). Subjects were treated with an average of 1.62mL (+0.76mL touch-up) of filler in the right temporal fossa and 1.47mL (+0.78mL touch-up) on the left side. Over the twelve-month assessment period, subjects reported moderate global aesthetic improvement and natural looking and feeling temples.[95] Significant improvement from Baseline was observed at all time points (Day fourteen, six weeks, three, six, nine, twelve months; $p < .05$), in all subjects, as per the MTVS. Investigators reported no serious complications but noted that 35% of subjects experienced discomfort while chewing and one subject developed a nodule. These AEs resolved within days and without sequelae, without the need for treatment. The authors concluded that calcium hydroxylapatite with lidocaine was found to be a safe and effective option to restore volume loss to the temporal fossa.

PLLA is a synthetic polymer that derives from the alpha-hydroxy family. When injected cutaneous, it is biocompatible but elicits an immunologic response. Following implantation, histological studies demonstrate that PLLA stimulates a fibroblastic response resulting in increased collagen production.[116] The aesthetic results of PLLA can last up to twenty-five months.[117] PLLA has been used to rejuvenate the temporal regions.[108,118] In a retrospective review of over 130 cases, injections of PLLA into the temporal region resulted in the highest subject satisfactions rates, in comparison to treatments of the cheeks (medial and lateral), tear troughs, nasolabial folds, marionette lines, chest, hands, and thighs. In addition, PLLA has been approved by the Food and Drug Administration (FDA) for the correction of facial lipoatrophy (FLA) in patients with human immunodeficiency virus (HIV).[119] In order to account for patient midface

differences at rest and in motion, a “smile-and-fill” technique has been adopted wherein the patient is instructed to smile and the needle is inserted into the accentuated malar cheek. The injector applies manual pressure of the PLLA following injection, to ensure equal distribution, followed by instructing the patient to massage the area of injection for 5 minutes, 5 times a day, for 5 days. Use of this technique results in a natural appearance of fullness in the face at rest, and a fuller midface appearance with facial movement, thereby avoiding the overfilled syndrome.

Non-permanent dermal fillers

Partially due to their proven safety and efficacy, HA dermal fillers are a popular option across aesthetic indications. In fact, HA is the most commonly used soft-tissue filler for any aesthetic purpose,[120] and temporal fossa restoration is often achieved with the use of HA.[121] Notably, comparative studies have revealed HA to be superior to autologous fat for treatment of temporal hollowing.[122] HA is a constitutive component of human skin and pharmacological preparations offer low reactivity and immunogenicity. Different formulations of HA gel fillers that vary in their HA concentration, particle size, cross-linking density, predicted duration, and inclusion/exclusion of lidocaine. Different formulations impact variable lifting capacity, firmness, and spreading.[123] Application of HA products varies according to the injector’s judgement. However, high-density, large-particle fillers are indicated for deep dermal injections while small gel particle fillers may be more appropriate for fine lines and shallow wrinkles.[124] HA treatments are typically quick and require little-to-no recovery time, with results lasting up to twelve to eighteen

months post-injection.[121] As different fillers vary in their physical properties and longevity, injectors are able to offer a great amount of flexibility when developing a treatment plan.

HA, calcium hydroxylapatite, and PLLA are indicated for similar aesthetic indications across the face (e.g., correction of facial wrinkles and folds). Generally, selection of a given product is at the injector's discretion and depends on the proposed use (i.e., depth of injection) and desired effect (i.e., sharp and sculpted versus subtle and natural).[125] It should be noted that no filler has FDA approval for use in the temporal region. Therefore, all uses of fillers (e.g., augmentation, lifting) in this region are considered off-label.[33] Nonetheless, the off-label use of injectable products such as HA, calcium hydroxylaptatite (e.g., Radiesse), and poly-L-lactic acid (e.g., Sculptra) to restore volume of the temporal fossa has become common in aesthetic practices.[95] Several recent clinical studies have aimed to quantify the safety and effectiveness of treating temporal hollowing with dermal fillers. A blinded, prospective, single-center, open-label trial in twenty subjects with moderate to severe temporal hollowness examined the use of small gel particle HA (Restylane®) for temporal fossa volumization.[90] Overall improvement in hollowness was reported in all subjects from month one to twelve, per the HSRS, and as evaluated by the patient, investigator, and a blinded physician assessor. No serious AEs (SAEs) were reported and all mild to moderate AEs resolved within two weeks. Based on these results, small gel particle HA demonstrated clinically significant efficacy and safety for use in temporal rejuvenation. A modified dilution and injection technique using HA fillers has also shown promise, with a dilution of two-to-one (saline to filler) resulting in more even distribution of the product in the temporal region.[126]

In an open-label, single-center study, thirty subjects were treated with an average of 1.1mL HA (Juvederm Voluma XC, 0.3w/w lidocaine), in each temporal region. At month 12, 98% of temporal regions displayed a ≥1-point improvement on the investigator-evaluated Frontal Temporal Fossa Scale. Most subjects perceived themselves as appearing younger after treatment. There was no correlation between jaw pain incidence and injection volume. Mild to moderate jaw pain during mastication was reported by 40% of study subjects post-injection. No vascular events or visual disturbances were observed.[121] Investigators noted that a "careful" injection technique was employed to reduce risk of SAEs, although they did not go into detail regarding what this meant. The authors concluded that the HA gel is safe and efficacious for use in the temporal fossa.

HA has also been used for the indication of FLA in patients with HIV. An open-label, safety and efficacy study saw improvement in HIV-associated FLA following midface volumization with HA for patients presenting with various levels of severity (ranging from grades 1-4, with higher scores indicating greater severity).[127] A mean volume of 6.1 to 9.3mL was used for grades 2 and 3 FLA. However, for grade 4 FLA which is nearing total fat loss and lipoatrophy of cheeks and temples, a total of 26.0mL was used. The authors concluded the safe and effective use of HA filler for the treatment of HIV-associated FLA.

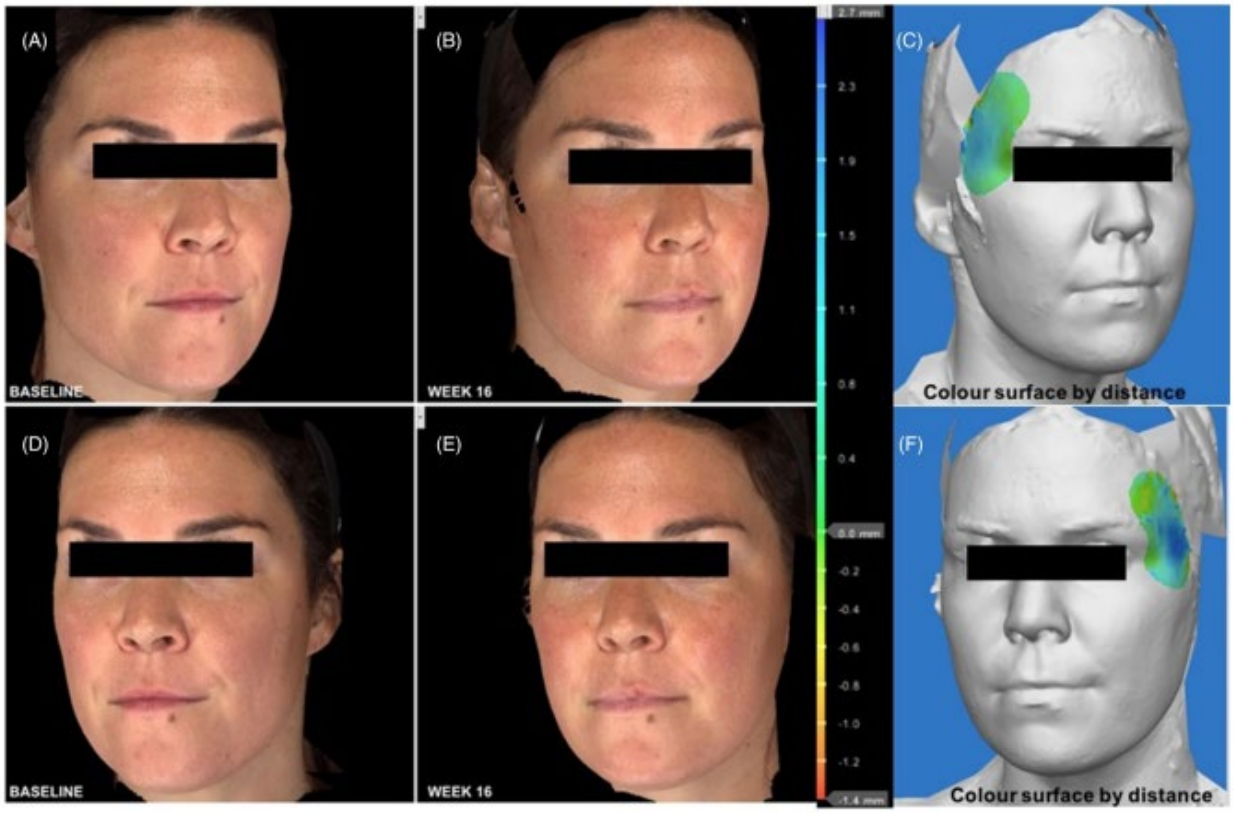
Indirect methods of volumizing the temporal region

Alternatively, temporal volume increase can be indirectly achieved following the injection of neuromodulators to the lower face. Nikolis et al[128] conducted a clinical trial

investigating the effects of botulinum toxin Type A for the treatment of masseter hypertrophy and observed concomitant temporal volume increase in a subset of subjects. This first of its kind observation in a clinical trial setting used physician assessments and objective 3D volumetric imaging to confirm a reduction in masseter hypertrophy accompanied by an increase in temporal fossa volume, with the blinded investigator reporting significant improvements in the temporal volume scale following single- and multi-injection techniques of botulinum toxin Type A. The mean unstratified volume increase after the treatment was 1.89 cc (SD: 2.0). The results led the authors to support the use of a full-face assessment for aesthetic procedures and suggest the use of neuromodulators in the lower face as a supporting option for achieving volumizing effects in the temporal fossa (Figure 27).

Figure 27

Indirect volumization of the temporal region



Note: Pre- and post-injection outcomes in temporal fossa volume with green demonstrating moderate (0.2-0.4 mm) increase in volume, and blue demonstrating major (1-2.7 mm) increase in volume. Copyright Nikolis, Enright, Rudolph, & Cotofana (2020).[128]

Adverse Events (AEs)

Generalized AEs

Temporal hollows can be effectively treated by volumizing the area using dermal fillers. However, AEs have been associated with these procedures. As such, the injector should be familiar with the signs and symptoms of AEs, and methods to their avoidance, management and treatment. Common AEs following dermal fillers are typically mild and transient in nature and can include bruising, swelling, dysesthesia (e.g., burning, prickling, tingling), and/or contour imperfections.[52] These AEs are primarily due to factors associated with the injection technique, rather than the product itself. For example, contour imperfections at or near the injection site can be due to too superficial or uneven placement of the filler.[48] Some investigators even consider suboptimal aesthetic outcomes to be considered AEs (e.g., Facial Overfilled Syndrome).[129]

The Tyndall effect refers to a bluish hue that results from placement of HA boluses that are too large or placed too superficially.[130] Discoloration results from the scattering of short wavelength light by HA particles. Thinning of the epidermis, as occurs with aging and is common in candidates for temporal fossa restoration, accentuates this discoloration. In addition, as relatively large volumes of product are typically required to restore volume of the temporal fossa, the risk for observing the Tyndall effect is increased compared to treatment in other anatomical areas. Discoloration associated with the Tyndall effect may resemble bruising, but unlike bruising it does not resolve in a matter of days unless pharmaco-mechanical therapy is administered. Hyaluronidase is typically used to dissolve excess HA, although alternatively, it may be excised.[131,132]

Temporary jaw pain and difficulty with mastication are frequently observed AEs following treatment of the temporal fossa.[95,121] The temporalis muscle, one of the primary muscles of mastication (along with the masseter, lateral pterygoid and medial pterygoid), spans from the temporal fossa to the inferior temporal line of the lateral skull.[133] Injection and filling of the fossa displaces the temporalis muscle, which may cause discomfort during chewing. This AE is typically noted immediately post-injection and resolves without treatment within a matter of days. Filler migration has also been reported in the literature, with material originally injected into the temporal region migrating to lower areas such as the orbital rim and cheeks.[134,135] Furthermore, the possibility of intracranial penetration while performing temporal injections has been proven. As the temporal region is a point of convergence for the sutures of the frontal, sphenoid, parietal, and temporal bones, authors have demonstrated that there are areas of bone instability where intracranial penetration can occur, with one suspected case having been reported in the literature previously.[136]

Vascular AEs

More concerning is the risk of SAEs, such as vascular compromise.[51,137,138] The temporal fossa has a complex anatomy due to multiple vessels running within different tissue layers.[139] In severe cases, accidental injection into veins can cause vascular compression or venous occlusion and arterial injections, embolization, skin necrosis, visual changes (e.g., blurry vision, blindness), stroke, or even death .[51,140] The pathway by which intravascular injection can lead to these SAEs is via filler embolism blocking end-arteries. Vessels without strong collateral circulation may pose increased risk, such as the supratrochlear artery.[131,141] While AEs may occur from any and all facial injections,

the specific anatomy of the temporal region may increase the risk of vascular SAEs, given that a rich, highly variable vascular network lies near the injection sites and communicates with the ophthalmic system.[48]

The face is not compartmentalized like other parts of the body, and vascular incidents are not regionally contained. Blood supply to the face is provided by the external and internal carotid arteries. Main arteries of the face originate directly from the external carotid artery (facial and superficial temporal arteries) or its branches (transverse facial artery from the STA, infraorbital artery from maxillary artery). These arteries cover the facial periphery while vessels supplied by the internal carotid artery (ophthalmic, supraorbital, supratrochlear, and dorsal nasal arteries) are confined to the center of the face.[25,46] Anastomoses unite these networks. Various veins, arteries, and nerves cross the face. All punctures interact with some part of the rich facial vasculature, but certain interactions lead to serious complications.[23]

Facial injection at various points has resulted in embolization into the ophthalmic artery followed by permanent and irreversible blindness.[142-144] Almost two-hundred cases of blindness following facial injection for aesthetic purposes have been reported in the literature.[142,143,145-150] More than half of these cases have occurred since 2012, reflecting the increasing popularity of aesthetic facial injections and parallel increase in serious complications.

To date, several cases of blindness have reportedly resulted from injection of the temporal fossa, specifically. Augmentation of the temporal region with silicone caused blindness in the eye of a 36-year-old woman treated in Thailand.[149] Notably, the use of silicone-based dermal fillers is not approved in North America. In the United States of

America (U.S.), the FDA strongly cautions against the illegal importation and unapproved use of fillers, noting that silicone injections can cause serious health consequences, including death ("The FDA Warns Against Injectable Silicone for Body Contouring and Enhancement," 2017). The first case of blindness following aesthetic facial injection to occur in the United Kingdom was reported in 2012. This patient was treated in the temporal region with PLLA,[151] which was not previously associated with any cases of blindness. The possible cause of blindness was suggested to be injection into the MTV, which drains into the STV.[112]

One Chinese study of thirteen consecutive patients with fundus artery occlusion caused by facial filler injections featured two patients who were treated in the temporal region.[152] Both patients were treated with autologous fat, though other treatment characteristics including needle diameter (0.3mm vs 2mm) varied. They were diagnosed with ophthalmic artery occlusion attributed to a retrograde embolic mechanism potentially via the STA. A six-patient case series on severe vision loss caused by cosmetic fillers featured one patient who experienced blurred vision of the left visual field and inability to elevate the left upper eyelid when her left temporal region was injected with 0.1mL of HA, using a deep bolus injection technique with the tip of the needle touching bone. Investigators concluded that the STA was likely injected inadvertently, and material travelled via terminal branch anastomoses with the supraorbital artery. Fortunately, in this case, treatment with hyaluronidase provided immediate relief and full recovery of vision was observed within one day.[153] Importantly, this is the only recorded case of full vision recovery following vascular compromise due to a filler-related complication.

Impact of current study on previous published reports of blindness:

Based on the description of the injection technique and location of product placement, the above case is an example of a possible error in the reporting of the pathway leading to the observed complication. The likelihood that the anterior DTA was involved must absolutely be considered and negated, prior to considering the involvement of the STA, which is located superficially to the site of injection and product placement. One must keep in mind that the anterior branch of the DTA anastomoses with the lacrimal artery through small branches which perforate the zygomatic bone and greater wing of the sphenoid.[154] Discussion with the senior anatomist on this case has led to an agreement of the alternate and more likely pathway of vision loss, leading to a letter to the editor in the near future.

A sixty-four-year-old woman experienced loss of vision, among other symptoms, following calcium hydroxylapatite injection of the bilateral temporal regions, cheeks, forehead, and chin.[155] This patient also experienced right-side periorbital ache and had notably more filler injected into the right temporal region than the left and developed significant hematoma at the right injection site. The authors hypothesized that arterial penetration involving the zygomaticotemporal artery had occurred, as inflammation of the lacrimal gland and the lateral rectus muscle were observed, and the zygomaticotemporal artery branches off the lacrimal artery. Similarly, the right temporal fascia was inflamed.

Blindness can occur if the retinal artery becomes occluded, attributable to either external pressure on the vessel or to occlusion by intravascular material. Compared to compression, intravascular occlusion is considered more likely, given the extensive arborization of vessels in this area.[112] The retinal artery does not need to be injected

directly. Filler injected into branches or anastomoses of the ophthalmic artery may enter the ocular circulation by retrograde arterial flow, eventually reaching the retinal artery. Retrograde arterial flow occurs when intravascular injection pressure exceeds intra-arterial pressure during intra-arterial injection and causes the filler to proximal to the central retinal artery. Once intravascular pressure is relieved, the embolic material moves distally and blocks blood supply. Blurring or loss of vision is immediate.[107,143] This effect is an application of “Poiseuille's Law,” which describes the velocity of the steady flow of a fluid through a narrow tube, such as a blood vessel or a catheter.[156] Experiments performed in six cadavers confirmed the existence of an embolic channel connecting the arterial system of the face to the ophthalmic artery.[144] Colored dye was observed to travel from the facial arteries to five ipsilateral globes and in three contralateral globes under conditions favoring embolism, demonstrating retrograde ophthalmic perfusion. Dye injection of the STA did not have this effect. Authors concluded that inter-arterial anastomoses between the face and the eye permit filler emboli to cause ocular complications. As instances of vision loss following aesthetic rejuvenation of the temporal fossa remain rare and typically only appear in case reports, the true incidence of their occurrence in unknown.

Injection techniques

Several injection techniques have been proposed for rejuvenating the temporal regions, including:

1. Subdermal injection (Layer 2)
2. Interfascial injection (Layer 4)
3. Low supraperiosteal injection (Layer 9)
4. High supraperiosteal injection (Layer 9)
5. Supraauricular injection (Layer 2)
6. Supra-SMAS injection (Layer 2)

Techniques 1-4 are ideal for *volumizing* the temporal regions, while techniques 5 and 6 are best suited for *lifting* the soft tissues of the region. Due to the highly vascular nature of the temporal region, pre-injection aspiration should be performed during all treatments.

1. Subdermal injection technique

In the subdermal injection technique, injectors place the product in the superficial or subdermal fatty layer of the temporal fossa (Layer 2). This layer consists of superior and inferior superficial fat pads, which are bounded by the zygoma. Given the location of the zygomatic arch, there is no risk for product displacement when HA is injected into the subcutaneous layer of the temporal fossa.[136] When performing this technique, authors have suggested placing the product in the superficial fatty layer of the anterior temporal region, using a 22G, 50mm obtuse tip cannula. The cutaneous passageway is the midportion of the zygomatic curve, wherein the cannula is progressed into the subdermal plane with the incline pointing to the dermis. The product is administered using a retrograde fanning technique, across the temporal area displaying volume loss. A low G-

prime material is considered most suitable for subdermal injections because high G-prime products can be noticeable due to the thinly overlying tissue. These characteristics make the subdermal layer suitable for both lifting and volumizing.[4]

Clinicians are partial to this technique because the cannula tip can become visible upon shifting it upwards to the skin, permitting injectors to verify the appropriate subdermal positioning. With deeper plane advancements, the cannula is less palpable. Furthermore, there are no major arteries in the subdermal layer. Vessels may become more apparent following treatment, possibly due to the increase in pressure following injection of HA. However, this usually resolves within two to seven days,[4] without intervention or sequelae.

2. Interfascial injection technique

In addition to volumizing the temporal region, the inter-fascial injection technique can elevate the position of the tail of the eyebrow. For performing this technique, the product is placed between the superficial and deep temporal fasciae (Layer 4). This layer can be accessed via the forehead or scalp, by advancing the cannula from a medial position to the temporal crest.[4] The tip of the cannula should be in contact with the bone during advancement. A 22G 50mm cannula is ideal for administering the product via a retrograde fanning technique. Care should be taken to avoid the MTV and frontal branches of the facial nerve, which are in the targeted plane.[4]

3. **Low supraperiosteal injection technique**

The low supraperiosteal injection technique is also referred to as the “one up and one over technique”.[157] In this technique, the needle access point is located 1cm cranially (“up”) and 1cm laterally (“over”) from the temporal crest. Using a 27 G sharp-tip needle, the product is placed in the supraperiosteal plane, within the temporalis muscle (Layer 9). The position of the tail of the eyebrow can also be elevated via this technique.

As this is an intramuscular injection technique, patients may experience post-injection headache or discomfort during mastication.[158] Injectors should be aware of the location and course of the anterior DTA, which is in close proximity to this location, in order to avoid accidental intravascular injection. Small volumes of a high G-prime product are best suited for this injection technique, as a low G-prime product may migrate into the orbit, middle, or lower face.[4]

4. High supraperiosteal injection technique

Compared to the low supraperiosteal injection technique, the high supraperiosteal injection technique places the product more cranially. Some authors theorize that this may also be a safer technique, as given their distal location from their emergence from the internal maxillary, the diameter of the arteries is smaller in this region.

The cutaneous access point for the high supraperiosteal injection technique is located 1cm inferior to the temporal crest in a vertical line 1cm posterior to the lateral bony orbit. A 27G sharp-tip needle is inserted perpendicular to the skin surface until bony contact is established and then tilted cranially by 45 degrees. As is recommended for

other injection techniques, a high G-prime product should be applied slowly, in small quantities (i.e., less than 1cc).

5. Supraauricular lifting injection technique

The supraauricular technique is primarily used for its lifting effects, which can extend to the mid- (including the peri-orbital and malar areas) and lower face. Therefore, the temporal region should be treated prior to treatment of lower facial regions. In this technique, the product is injected into the subdermal plane (Layer 2) of the posterior temporal region. The access point of the needle is in the anterior third of the zygomatic arch, lateral to the line of ligaments. A blunt tip 22G 50mm cannula is introduced into the superficial fatty layer with the bevel facing upwards and advanced toward the superior aspect of the auricle. Tilting the cannula against the underside of the dermis can be used to ensure correct positioning in the subdermal plane.

6. Supra-SMAS injection

In the supra-SMAS injection technique, product is placed within the subdermal plane (Layer 2) of the posterior temporal region. This technique is used exclusively for its lifting effects, as this area is covered by hair and does not exhibit any appreciable volume loss. The needle point is accessed 1 cm anterior to the apex of the tragus. A 22G 50mm (alternatively, 70mm may be used) blunt-tip cannula is inserted into the subdermal plane with the bevel of the cannula pointing up toward the dermis. Special attention is required to avoid displacement of the cannula into deeper planes. Importantly, the initial description of the technique as “supra-SMAS” has been proven incorrect, as the SMAS

is not present in this region. Instead, authors now refer to this technique simply as the "temporal lifting technique".[4,85]

Given the above-mentioned techniques, there are three potential planes for augmentation of the temporal fossa: (1) The immediate subcutaneous plane (superficial to the superficial temporal fascia), (2) just deep to the superficial temporal fascia (between the superficial and deep fascia), and (3) deep to the temporalis muscle.[157] The previous literature has suggested that HA-based fillers should be placed in either the subcutaneous plane or deep to the temporoparietal fascia, whereas collagen-stimulators (e.g., PLLA or calcium hydroxylapatite) should be placed deep to the temporalis muscle.[90,159] However, other authors argue that HA fillers are most safely placed deep to the temporalis muscle, directly on periosteum.[33] Based on their cadaveric and CT assessments, Chen et al[44] proposed that the safest planes with the fewest vessels are the periosteum and the loose areal tissue. The authors suggested that sharp needles are best used in the plane periosteum and subcutaneous tissue, whereas blunt cannulas should be used when injecting into the loose areal tissue.

A recent retrospective image analysis was performed by Casabona et al[160] wherein the supraperiosteal, inter-fascial and subdermal injection techniques were compared.[160] The supraperiosteal injection technique was found to be superior compared to the other techniques with regards to improving temporal volume, temporal crest and lateral orbital rim visibility. The inter-fascial injection technique demonstrated the greatest impact on correction of crow's feet and eyebrow positioning, while the subdermal technique showed the greatest effect in the lower face and lateral midface. The authors concluded that the strengths and weaknesses of each injection technique should be considered, and

injection method should be chosen according to the patient's aesthetic needs. Future utilization of a *multi-layer injection approach* is possible, wherein all three injection techniques are tailored for a single patient, based on the desired outcomes. However, this study only compared three of the six presented injection techniques. Thus, additional studies are warranted.

Despite attempts to inject within the intended plane(s), errors can occur (Box 3). For example, in one study, injectors attempted to place HA within the temporal fat pad, but post-injection US confirmed that in 10% of specimens, the product was located one layer deep, within the temporalis muscle. The authors speculated that this inaccuracy was likely related to advancement of the needle from digital pressure during injection.[161] In another study, researchers used cadavers to elucidate the location of HA gel after subcutaneous injection into the region of temporal hollowing. Histology confirmed relatively consistent placement of the gel within the subcutaneous tissues, but unintended deeper location of filler and significant perivascular collection of the material was also found. This led the authors to conclude that injection into the subcutaneous plane may be associated with increased risk of vascular events.[8]

Box 3
Reasons AEs Can Occur Despite Proper Knowledge and Expertise

- Inaccurate or unknown subject history (e.g., past injections, scarring, surgery).
- Technical considerations while performing injections (e.g., force of injection, speed of injection, diameter of needle/cannula).
- Local trauma, infection (e.g., dental, sinus, or vaccine triggers).
- Patient manipulation of region.
- Variant of normal anatomy.

Signs and symptoms of vascular adverse events

Initial signs and symptoms of vascular occlusion may include erythema, bruising, pain, and swelling; and these can be mistaken for being an injection-related AE.[113] Injection site reactions such as erythema, edema, tenderness and bruising are common, mild AEs that resolve quickly.[162] On the other hand, vascular occlusion frequently presents with sudden, severe pain accompanied by a visible pallor or skin blanching that later develops into blotchy, mottled discoloration known as livedo reticularis;[6,33,163] with skin changes occurring immediately or within hours after injection.[162] The area of ischemia may also display deep blue petechiae and an erythematous patch. Failure to treat the early warning signs of vascular occlusion can lead to the development of necrosis.[33,164] The first patient case of filler-induced necrosis and subsequent alopecia was reported in 2013 following temporal augmentation.[165] More recently, a similar case of bilateral injections to the temporal region led to reversible alopecia with localized scalp necrosis.[166] In both reported cases, the HA doses administered (6-6.5 mL in each temporal region) exceeded the recommended safe HA filling dose (0.5-3 mL per temporal region) and may have increased the risk of compression-induced tissue ischemia. It is important to recognize intravascular necrosis as soon as possible and respond with appropriate treatment to prevent further complications.[6]

Signs and symptoms of visual impairment following facial filler injections can include ptosis, ocular pain, nausea, headache, dizziness and skin necrosis.[167] Cases of disturbed ocular mobility, corneal edema, dilated pupils, hypopyon hyphema (pus or blood in the eye) and iritis have also been reported, with the worst vascular AEs being residual tissue loss, visual and neurological sequelae. There have been several reports in the

literature of these complications resulting from inadvertent injection of various materials (e.g., adipose, poly-L-lactic acid, calcium hydroxylapatite, HA) into the temporal arteries, followed by anterograde or retrograde delivery to the orbital and/or cerebral arteries.[136,168-170] For example, one patient developed blurred vision and the inability to elevate the upper eyelid immediately after filler injection into the left temporal area. However, the patient's visual loss was fully restored following proper treatment and management of symptoms.[153] The authors speculated that this particular AE was likely caused by the placement of the injection in the frontal branch of the STA.

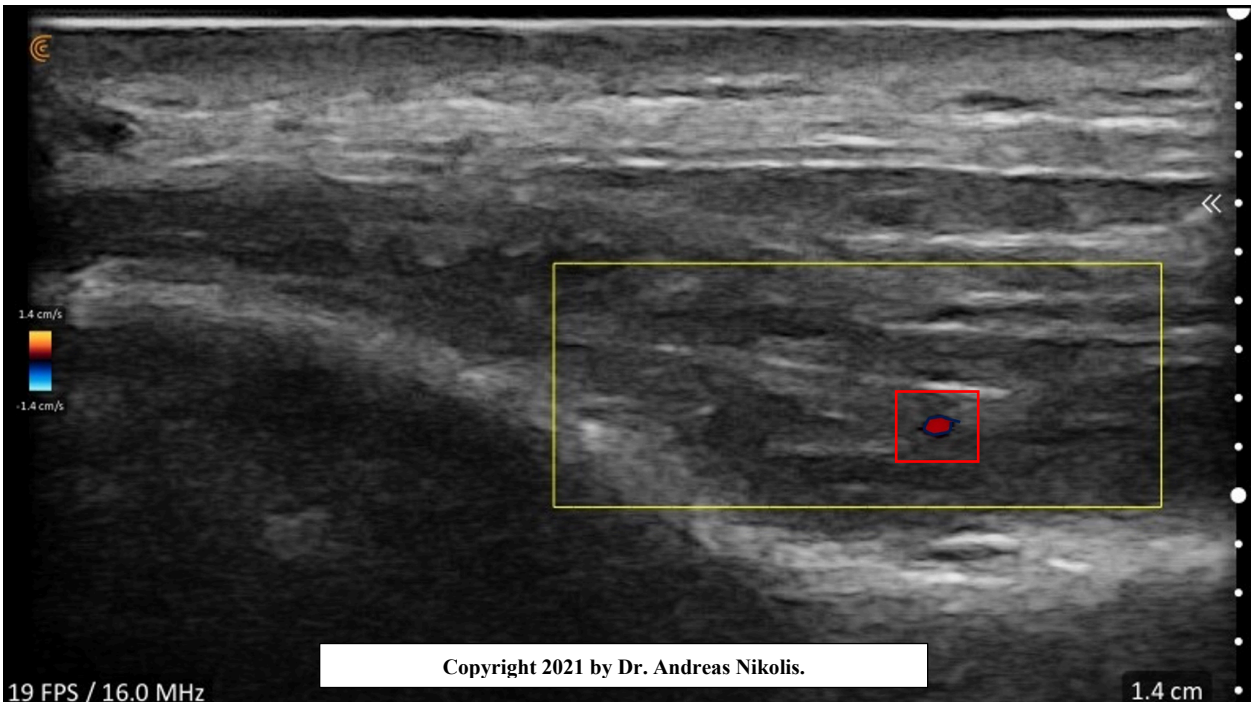
Avoidance of vascular adverse events

Various strategies have been recommended to reduce the risk of vascular complications following HA injection.[153] Detailed knowledge and understanding of facial anatomy and plane of injection remains at the forefront, with an emphasis on vascular anatomy and variation. Injection technique is also critical (e.g., slow rate of injection with small aliquots of product). The use of a blunt cannula or small needle is also recommended for volumizing the temporal region. Additionally, patient medical history including previous cosmetic or surgical procedures must be considered to ensure safety and efficacy of the treatment. An undebated key element to avoiding SAEs associated with injecting soft tissue fillers in the temporal region is a thorough understanding of the relevant vascular anatomy. Pre-treatment vascular mapping may be useful in the temporal regions, where individual anatomical variations in vital vascular structures are abound and arborizations remain highly variable. The use of non-invasive, high frequency ultrasound imaging (HFUI) can be employed prior to injection to visualize the skin,

underlying tissue (e.g., fat, fascia, muscles) and vital vascular structures (i.e., veins and arteries).[171-173] By examining pre-injection HFUI, vital vascular structures can be avoided during injection. HFUI can also be used during the injection, to guide treatment and improve outcomes. Investigators recently (2021) reported the ability to avoid injecting into the superficial temporal branch of the facial artery, the zygomatico-orbital artery, and the DTAs in all study subjects undergoing temporal volumization, by identifying these structures with HFUI.[48] In addition, HFUI can be used to confirm injection into the correct plane. The use of a B-scan US combined with color doppler US (known as duplex sonography) can also be used to detect movement of blood within vessels to help distinguish structures. Moreover, the direction of blood flow can be identified using Color Doppler (blue vs red) for additional analyses (Figure 28). Although US-guided interventions can help improve outcomes, these technologies are limited by cost and require specific training for use. It is therefore important to identify clear clinical landmarks to guide clinicians during filler injection and minimize risk of AEs.

Figure 28

Color Doppler Ultrasound Image Displaying Speed and Direction of Blood Flow Within the Deep Temporal Artery



Note: Color doppler ultrasound (Manufacturer: Clarius; Model: L20 HD). The deep temporal artery is not directly on bone and can vary in position within the deeper layers of the temporalis muscle. The color doppler function of an ultrasound displays flow towards the transducer in red (box) and flow away from the transducer in blue. Lighter shades of color are assigned to higher velocities. Copyright 2021 by Dr. Andreas Nikolis.

Safety concerns regarding treatment of the temporal region have been raised due to its proximity to the ophthalmic artery, as obstruction may lead to blindness.[112,113] More specifically, the concern arises from the crossover arborization of the supraorbital and supratrochlear arteries that have retrograde flow to the retinal branch of the ophthalmic artery. Systolic pressure must be overcome to achieve retrograde flow of product down the arterial system. Therefore, product should always be injected slowly and steadily without significant force.[135]

Different areas have different risks of vascular complications pertaining to the existence of the underlying core vascular structures of that facial soft tissue subunit. Authors have suggested to avoid injecting parallel to the inter-fascial space, that is, between the superficial and deep temporal fasciae, as the middle temporal artery emerges within this plane and can lead to hematoma or chronic headache if injected.[4] There is also an inherent risk of injury or paralysis to the frontal branches of the facial nerve when injecting into this region, which may lead to temporary brow ptosis. Goodman et al[174] recommend avoiding injecting into mimetic muscular layers, as this may produce product clumping, displacement, and tendency for late nodularity swelling.[174] A safe injection zone has been previously outlined by Tansatit et al[38] as the intersection of the temporal and the frontal processes of the zygomatic bone at the posterior angle of the zygoma. The maximum depression of the temporal region that is undergoing correction typically resides in this area, allowing it to serve as a landmark for safe injection. Injecting outside of this defined safety zone may increase the chance of MTV cannulation and fail to provide further benefits from the filler. Yang et al[28] proposed using the Valsalva maneuver to identify the MZTV and sought to clarify the anatomy and course of the MZTV

in order to identify superficial landmarks, a technically difficult procedure. However, the authors found that simple palpation or inspection could not identify veins entrapped by muscle. For example, in 83.3 % of cadavers analyzed, the MZTV was entrapped by the orbicularis oculi muscle. Therefore, the use of superficial landmarks as references for the location of the MZTV are critical in enhancing the safety of injectable treatment procedures.[28]

The important role of tributaries is displayed by the observation that temporary compression of the main hazardous channels can limit AEs.[38] Pressing the pre-tragal confluent point during anterograde temporal injections can be used as an avoidance method for vascular risks. Another potential AE-preventative maneuver regards compression of the orbital rim at the superior nasal corner which can retard ocular infusion in arterial injections.[144]

Knowledge on vascular anatomy in the temporal region can also be used as an AE avoidance tool. In the Chen et al[44] manuscript, they identified four arteries of the temporal region (STA, MTA, zygomatico-orbital artery and posterior DTA) and used these to divide the temporal area into four parts (A, B, C, and D). Interestingly, these arteries were found to pass through parts A, B, C, and D at probabilities of 30.73%, 37.06%, 39.48%, and 77.18%, respectively. In particular, the posterior DTA was found in a prominent and fixed position, with all its branches occupying the temporal region at the midpoint of the zygomatic arch. The upward direction of the posterior DTA enables communication with the MTA near the center of the temporal region, providing a blood supply to the temporalis muscle. These findings reveal the potential risk of encountering posterior branches of the DTA during temporal injections. Given this model, the authors

suggest that a needle can be placed in an area to minimize the probability of injecting filler into a blood vessel. Importantly however, no area of the temporal region was found to be completely safe, with the “safest” area (part A) carrying an over 30% probability of containing a major artery. The validity of this model is debatable as the anterior branch of the DTA was not mentioned.

HA fillers can undergo enzymatic reversal via the direct or diffuse injection of hyaluronidase. However, no dissolving agent or antidote exists for permanent or semi-permanent fillers (e.g., collagen, paraffin, polymethyl methacrylate, silicone, autologous fat, calcium hydroxylapatite, poly-L-lactic acid).[48] Given the severe nature of some AEs, their impact on the patient’s quality of life, and the limited availability of reversing agents, prevention is of paramount importance.

As described above, many recommendations have been published to diminish intravascular deposition of product,[113,175] including pre-injection aspiration, which can be used to demonstrate intravascular placement of the needle.[113] The presence of blood upon withdrawal of the syringe would indicate improper intravascular placement of the needle and require repositioning. However, the use of pre-injection aspiration is frequently debated in literature. Cases of vascular complications occurring even after negative aspiration has led some authors to be skeptical of its value.[176] The inability to retrieve flashback into a syringe may be due to the combinatory use of thick gels and fine needles.[175] Additionally, the efficacy of this technique is limited for facial filler injections due to the small size and collapsibility of facial vessels.[177] A comparative study of withdrawal using a series of needles and various commercial HA fillers failed in most cases, revealing gel properties (e.g., high G prime and high cohesivity) and needle size

(i.e., smaller gauge needles or needles pre-supplied with product) to impact negative aspiration. Authors concluded that intraarterial position of the needle cannot be confirmed using aspiration. Although recent consensus guidelines have warned against the use of aspiration for preventing against HA embolic visual loss, due to lack of evidence as a safety measure,[178] none of their observations were based on clinical trial data. Authors have argued that in the occurrence of a negative aspiration, the injector may have a false sense of security and proceed with a potential intravascular injection. Nevertheless, several authors continue to recommend pre-injection aspiration in hopes of minimizing the risk of intravascular placement,[112,113,175,179] including expert consensus recommendations.[180] A recently completed study evaluating the use of HA fillers in non-surgical rhinoplasty has demonstrated a greater than 10% chance of positive aspiration. This data should lend credence to the need for aspiration when injecting the face (Submitted 2021: Nikolis A et al., Prospective evaluation of safety and efficacy of medical rhinoplasty).

Management and treatment of vascular adverse events

As no single injection technique or combination of preventative measures is failsafe, injectors need to be equipped with a knowledge of S/AE management and treatment strategies. Post-injection, US can be used to evaluate whether there is a reduction in the volumetric flow of blood through arteries, to confirm vascular compromise; or following the administration of hyaluronidase to confirm the return of normal blood flow.[181]

With regards to retinal artery embolization, current literature has failed to provide a gold standard for its treatment.[153] However, it is important that every possible attempt is made to dissolve the embolized filler and fully restore vision. Upon immediate suspicion of ophthalmic artery occlusion, cessation of the injection procedure must occur, followed by administration of hyaluronidase in the treatment area, with possible supratrochlear/supraorbital hyaluronidase injection. Ocular massage and carbonic anhydrase inhibitors may also be used to lower intraocular pressure and restore retinal circulation. The patient must be promptly transferred to a specialist and possibly practice re-breathing into a plastic bag while being transferred to increase carbon dioxide for subsequent vasodilatation. Topical application of nitroglycerin paste (2%) has also been recommended as an early management strategy of arterial occlusion.[182,183] Nitroglycerin has vasodilatory effects on small-caliber arterioles, enabling its use to improve blood flow in compromised dermal vasculature.[184] However, the use of topical nitroglycerin may pose risk to the patient by worsening ischemia through dilation of vessels and further propagation of filler product into the small arterioles and capillaries; It may also onset systemic effects such as hypotension and dizziness.[185] Systemic steroids have also been suggested as an anti-inflammatory treatment for early presenting cases of vascular compromise.[138] Additionally, treatment with hyperbaric oxygen therapy can help increase oxygen delivery. However, the time to treat and manage retinal artery occlusion is of paramount importance. Unfortunately, patients experiencing blindness for more than 4 hours have shown unsuccessful restoration of visual acuity, even after high-dosage hyaluronidase treatment (1500-3000 units). Immediate action must therefore be taken for these patients to reverse blindness.

No safe and reliable treatment currently exists for the treatment of iatrogenic retinal embolism.[180] Lowering intraocular pressure would theoretically dislodge the embolus into more peripheral vessels. Diffuse injection of hyaluronidase into ischemic tissues may prove effective for emboli occurring post-HA injection.[163] Gentle pumping or massage may help to dissolve blockages and warm compress may be applied to encourage vasodilation. Topical nitroglycerin paste applied to the affected area may similarly support vascular dilation, but this region is not accessible to topical treatments, thus potent systemic vasodilating agents may be administered in a hospital setting.[186] Prostaglandin E1 promotes vasodilation and has proven effective in acute retinal artery embolism.[187,188] Treatment with hyperbaric oxygen in addition to other methods may produce better outcomes.[189,190]

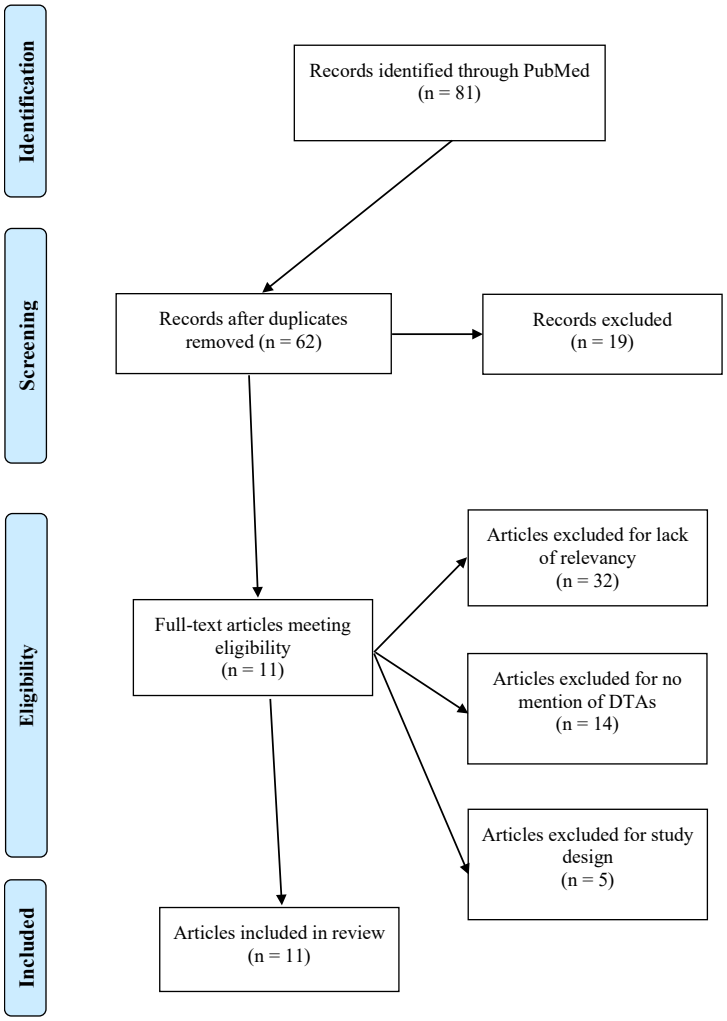
Project B- Systematic review of the literature and DTA landmarking

As briefly mentioned in the section entitled “The Deep Temporal Arteries”, one area where there is a major paucity of literature is with regards to the topography of the DTAs and their implications for performing safe aesthetic injections. In an attempt to prevent vascular AEs originating from injections into the temporal regions, the scarcity of treatment guidelines to date have focused primarily on avoiding the superficial and middle temporal arteries,[13,33,34] with reports infrequently discussing the role of the DTAs in relation to performing safe aesthetic treatments with fillers. Therefore, the aim of the following section will be to present a review and anatomical study that were undertaken to describe the topography of the DTAs with reference to superficial landmarks, to aid clinicians in performing safer temporal fossa injections.

Further evaluation of data for the region in question led us to perform a systematic review of the published medical literature, to ascertain the anatomical details of the DTAs. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Figure 29) were used in this review. Eligible articles for selection included original research articles, posters/abstracts, case reports/series, expert opinion, guidelines, and consensus papers published between January 1980 and September 2021, that investigated or discussed the anatomy of the DTAs. Articles excluded from this study included non-English language papers, duplicate papers, studies on animal models, and papers without mention of the DTAs. PubMed was used as the primary search engine, with Google Scholar as a secondary source. The search was conducted using the following keywords: “deep temporal artery fillers”, “deep temporal artery hyaluronic acid” and “deep temporal artery injectables”. The full texts of all articles were screened for inclusion. Two reviewers performed the screening and data abstraction processes independently and resolved any discrepancies through discussion. Relevant information regarding the anatomy of the DTAs were extracted from all included articles, using data abstraction forms. The findings of the systematic literature review were presented in the form of a table and narrative summary.

Figure 29

Results of the Systematic Literature Search for Published Articles Investigating or Discussing the Anatomy of the Deep Temporal Arteries (DTAs)



Note: From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by A. Nikolis, K. M. Enright, T. Troupis, et al., 2021.

The systematic literature search of articles investigating or describing the DTAs published between January 1980 and September 2021 yielded eighty-one articles. Nineteen duplicate articles were removed. Thirty-two articles were excluded for lack of relevancy to the topic of interest (i.e., anatomy of the DTAs), fourteen were removed for containing no mention of the DTAs, and five were removed due to study design (i.e., animal studies). After applying the inclusion/exclusion criteria, eleven publications were selected for review in the present study (Figure 29; Table 1). Full texts were available for ten articles, while only an abstract was available for one study. A majority (10/11; 90.90%) of study designs included cadaveric dissections, with only one publication reporting the results of a clinical evaluation.[191] Few articles (2/11; 18.18%) related the anatomy of the DTAs to injectable treatments.[44,191]

Table 1

Summary Results of the Systematic Literature Search on Previous Investigations and Scientific Descriptions of the Deep Temporal Arteries

Article Nº	First author	Citation	Study type	Topic	Sample	Major anatomical findings of the
1	Corrêa MB	Ital J Anat Embryol. 2008 Apr-Jun;113(2):109-15.	Cadaveric study (abstract only)	Reconstructive and reparative surgery	Twenty-one hemi-faces from cadavers of children (13 male and 8 female)	The trunk of the maxillary artery separates into anterior, posterior, and sometimes, accessory DTAs
2	Lee W	J Cosmet Dermatol. 2021 Sep 24.	Clinical evaluation using doppler ultrasonography	Aesthetic injectables	Thirty adult female patients (60 temples)	The anterior DTA was located under the temporalis muscle, very close to the surface of the temporal bone

3	Chen CL	Aesthet Surg J. 2021 Feb 27:sjaa371.	Cadaveric study using 3D reconstructions of CT images	Aesthetic injectables	Fifty-six adult cadaveric heads (107 sides), including 15 females and 41 males	The posterior DTA ran along the periosteum of the skull, with some anastomoses with the MTA
4	Beheiry EE	Plast Reconstr Surg. 2007 Jan;119(1):136-144.	Cadaveric study using radiography to delineate vasculature	Reconstructive surgery	Forty-four specimens (2 stillbirths and 20 embalmed cadavers)*	Branches of the STA communicate with the deep temporal arterial network
5	Ali A	J Plast Reconstr Aesthet Surg. 2012 Mar;65(3):e54-9.	Cadaveric study	Reconstructive surgery	Eleven Caucasian adult cadavers (5 male and 6 female) provided 17 dissections (6 bilateral and 5 unilateral)	The arterial supply to the deep surface of the temporalis emerged from the anterior and posterior DTAs and MTA. The positions of the DTAs relate to the location of the deep temporal nerve

6	Veyssiere A	Surg Radiol Anat. 2013 Sep;35(7):573-8.	Cadaveric study	Reconstructive surgery	Seven fresh cadavers (14 dissections)*	The vascularization of the temporalis muscle is provided by the DTAs (both collateral branches of the internal maxillary artery), and the MTA (a collateral branch of the STA)
7	Kim S	J Craniofac Surg. 2005 Jul;16(4):651-4.	Cadaveric study	Neurosurgery, plastic, cosmetic, maxillofacial, and head and neck surgery	Eight fresh-frozen cadaveric heads (4 female and 4 male) provided 15 dissections	The arterial supply of the superficial fat pad arises from the DTAs and MTA

8	Nakajima H	Br J Plast Surg. 1995 Oct;48(7):439-50.	Cadaveric study	Reconstructive surgery	Ten fresh cadavers*+	The anterior and middle portion of the temporal muscle is supplied by the anterior and posterior DTAs. Most of the posterior portion of the temporal muscle receives its blood supply from the MTA

9	Elazab EE	Surg Radiol Anat. 2006 Jun;28(3):241-7.	Cadaveric study	Reconstructive surgery	Same sample as Nº 4 (Beheiry, 2007)	The presence of anastomotic vessels between the superficial and deep temporal vascular systems, traversing the loose areolar fascial plane, was confirmed. The anterior and posterior DTAs lay deep to the anterior and the middle thirds of the temporalis muscle

10	Chen CT	Plast Reconstr Surg. 1999 Apr;103(4):1181-8.	Cadaveric study with macroscopic and radiographic evaluation	Reconstructive surgery	Six fresh cadavers provided 12 dissections (3 males, 3 females)	The anterior and middle portions of the reverse temporal muscle were mainly supplied by the DTAs, whereas the proximal two-thirds of the posterior portion was furnished by the MTA.
11	Burggasser G	Plast Reconstr Surg. 2002 May;109(6):1862-9.	Cadaveric study	Reconstructive surgery	Sixty Caucasian cadavers (27 male and 33 female)[+]	The DTAs and MTA supply the temporalis. The DTAs follow the edge of the temporalis, between the muscle and bone

Note: DTA = Deep temporal arteries; MTA = middle temporal artery; STA = Superior temporal artery. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections” by A. Nikolis, K. M. Enright, T. Troupis, et al., 2021. *Gender of specimens not reported. [+]Number of dissections not reported.

One study investigated the vasculature of the temporal region via dissection of twenty-one hemi-faces from the cadavers of children (thirteen male and eight female). The trunk of the maxillary artery was found to separate into an anterior, posterior, and sometimes, accessory DTAs. The anterior DTA originated in front of the coronoid process, while the posterior DTA originated behind the coronoid process. The most frequently observed arterial branch in the anterior third of the temporal muscle was the anterior DTA; in the middle third, it was the posterior DTA; and in the posterior third, it was the middle temporal artery.[192] These findings expanded on an earlier study that reported that the anterior and middle portion of the temporal muscle was supplied by the anterior and posterior DTAs, while most of the posterior portion of the temporal muscle received its blood supply from the middle temporal artery.[193,194] Similarly, additional cadaveric studies revealed that the vascularization of the temporalis muscle originates from the anterior and posterior DTAs (both collateral branches of the internal maxillary artery), and the middle temporal artery (a collateral branch of the superior temporal artery);[195] and the arterial supply of the superficial fat pad arises from the DTAs and middle temporal artery.[196]

A recent clinical evaluation attempted to use doppler US to detect any anatomic variations in the blood vessels of the commonly used injection site of the temporal region (i.e., 1cm lateral and 1cm above from the end of eyebrow). These researchers observed that the anterior branch of the DTA was located under the temporalis muscle, very close to the surface of the temporal bone. However, they could not locate the posterior DTA in any of the subjects, using US.[191] Conversely, a recent cadaveric study using 3D reconstructions of CT images from fifty-six cadaveric heads was able to locate the

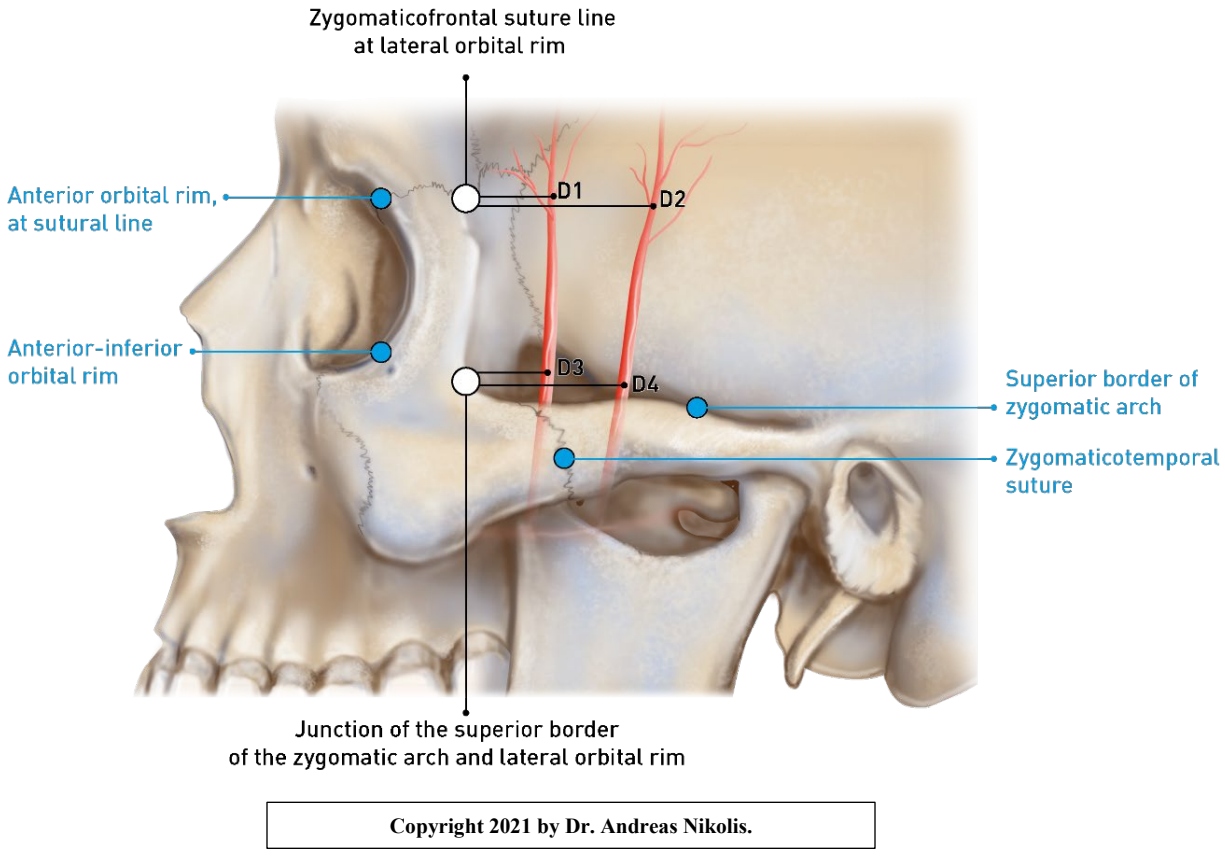
posterior DTA but made no mention of the anterior DTA. The posterior DTA was found to arise from the maxillary artery and ran into the temporal region at the midpoint of the zygomatic arch, after which it ran directly upward. The posterior DTA ran along the periosteum of the skull, with some anastomoses with the MTA near the center of the temporal region, providing a blood supply to the temporalis muscle.[44] Another cadaveric study using radiography to delineate vasculature confirmed the existence of anastomosing vessels between the superficial and DTAs, which passed through the loose areolar and deep temporal fasciae.[197,198] The locations of the anterior and posterior DTAs have also been found to relate to the location of other important nearby structures. For example, the posterior DTA was found deep and posterior to the deep temporal nerve in 65% of observed specimens.[199]

To identify the location of the DTAs in relation to pre-defined anatomic landmarks, the temporal fascial layers of eight fresh frozen, non-embalmed cephalic specimen were dissected and assessed, bilaterally. The body donors included in this study were 100% Caucasian males with an average age of 69.62 years (SD: 2.82)]. Body donors were screened for exclusion criteria, including previous facial operations, trauma, or disease-associated abnormalities in facial anatomy. While alive, donors provided informed consent for the use of their body for medical, scientific, and educational purposes. All dissections were guided by red latex injections into the arterial vascular system and were performed by the same two surgeons to assure consistency throughout the measurements. The distance (D) to the anterior (D1 and D3) and posterior (D2 and D4) arteries were measured from i) the zygomaticofrontal suture line at the lateral orbital rim (D1 and D2) and ii) the junction of the superior border of the zygomatic arch and lateral

orbital rim (D3 and D4). The distance between the anterior and posterior DTAs were also recorded, at the level of the zygomaticofrontal suture (D5; Figure 30).

Figure 30

Distance Between Anterior and Posterior Deep Temporal Arteries

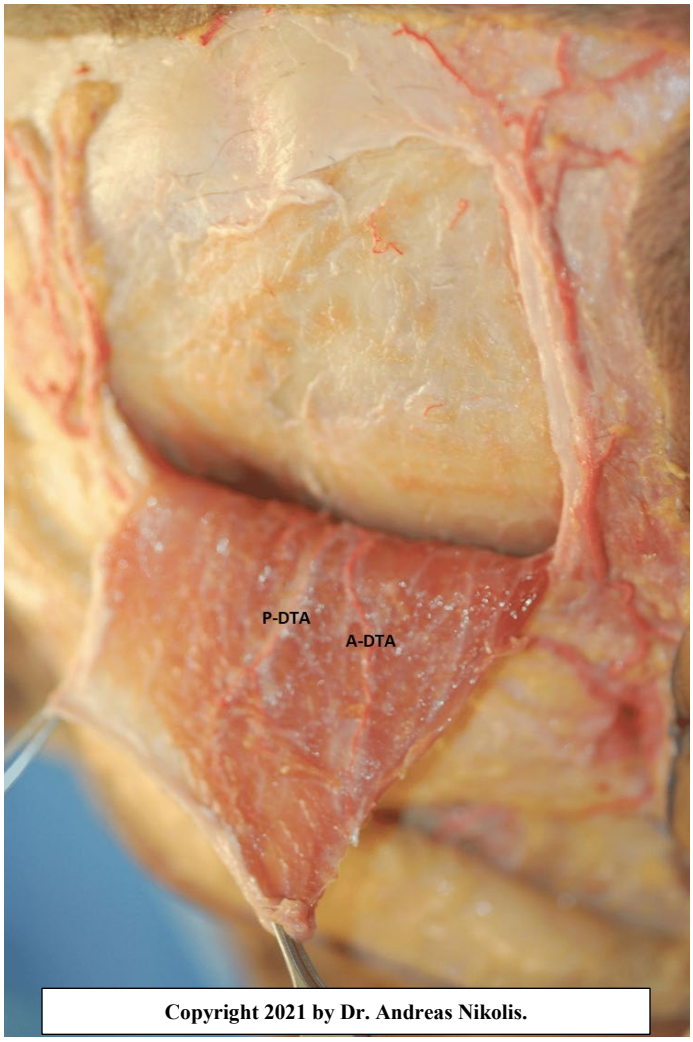


Note: The distance (D) to the anterior (D1 and D3) and posterior (D2 and D4) arteries were measured from i) the zygomaticofrontal suture line at the lateral orbital rim (D1 and D2) and ii) the junction of the superior border of the zygomatic arch and lateral orbital rim (D3 and D4). The distance between the anterior and posterior DTAs were also recorded, at the zygomaticofrontal suture level (D5). From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

The DTAs were found bilaterally in all cadavers. In all cases, the DTAs were located in the deepest part of the temporalis muscle, superficial to the periosteum (Figure 31). Table 2 displays the distance (cm) between standard anatomical landmarks [e.g., i) the zygomaticofrontal suture line at the posterior orbital rim, and ii) the superior border of the zygomatic arch and lateral orbital rim junction] and the anterior and posterior branches of the DTA at the level of the zygomaticofrontal suture. On average [mean (standard deviation)], D1 = 1.56cm (0.59); D2 = 2.98cm (0.70); D3 = 1.14cm (0.63); D4 = 2.37cm (0.62); and D5 = 1.41cm (0.75).

Figure 31

Deep Temporal Arteries are Located Under the Temporalis Muscle



Note: The classical branching pattern of the DTAs occurred in 68.75% (11/16) of cases and consisted of an anterior (A-DTA) and posterior (P-DTA) branch. In all observed cases, the DTAs were located deep in the temporalis muscle, superficially to the periosteum. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

Table 2

Distance (cm) of the Anterior and Posterior Branches of the Deep Temporal Artery in Relation to Standard Anatomical Landmarks

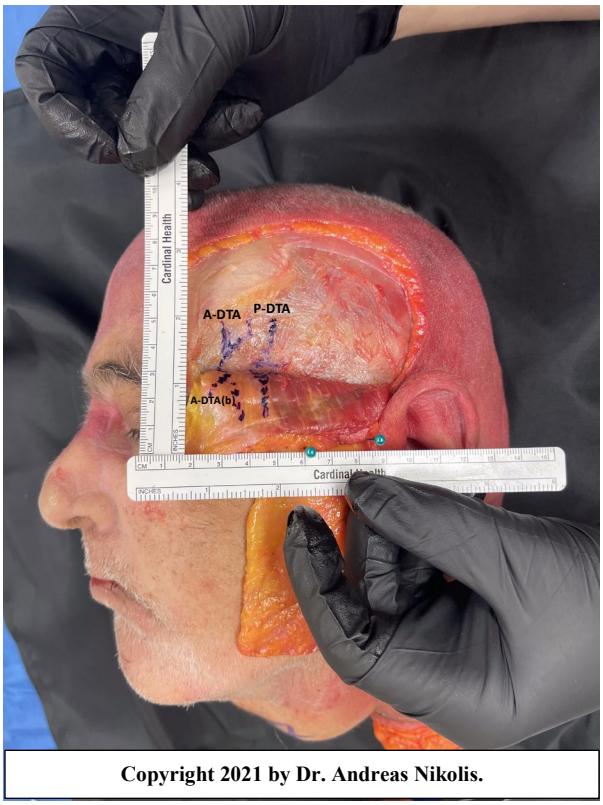
Specimen Nº	D1	D2	D3	D4	D5	Anatomy
1	1.6	3.2	1.4	3.2	1.6	Type 1
2	2	3.6	1.5	3	1.6	Type 2
3	1.6	3.3	1.2	2.9	1.7	Type 1
4	1	1.8	0.7	1.5	0.8	Type 1
5	1.2	1.9	0.8	1.6	0.7	Type 3
6	2.4	3.3	1.5	2.8	0.7	Type 3
7	1.2	2.3	1	2	1.1	Type 1
8	1	2.8	0.6	2	1.8	Type 1
9	0.9	2.4	0.6	1.7	1.5	Type 2
10	1.9	3.9	2.6	3.2	2	Type 1
11	0.9	3.9	0.4	2.4	3	Type 1
12	0.8	2.2	0.6	2	1.4	Type 1
13	2.4	2.8	1.5	1.8	0.4	Type 1
14	1.3	4.2	0.3	3.3	2.9	Type 1
15	2	3	1.3	1.8	1	Type 1
16	2.7	3.1	2.3	2.7	0.4	Type 2
Mean (SD)	1.56cm (0.59)	2.98cm (0.70)	1.14cm (0.63)	2.37cm (0.62)	1.41cm (0.75)	N/A

Note. D = Distance; D1 = Zygomaticofrontal suture line at lateral orbital rim, to anterior DTA; D2 = Zygomaticofrontal suture line at lateral orbital rim, to posterior DTA; D3 = The junction of the superior border of the zygomatic arch and lateral orbital rim, to anterior DTA; D4 = The junction of the superior border of the zygomatic arch and lateral orbital rim, to posterior DTA; D5 = The distance between the anterior and posterior branches of the DTA, at the level of the zygomaticomaticofrontal suture. Branching Type 1 = DTAs consisted of an anterior and posterior branch; Type 2 = The anterior DTA displayed bifurcations; Type 3 = The posterior DTA displayed bifurcations. SD = standard deviation. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

Three branching patterns from the stem of the DTAs were observed (Figures 31-33). Classical branching into frontal (anterior) and parietal (posterior) arteries was seen in 68.75% (11/16) of cases. Bifurcating frontal and posterior branches were reported in 18.75% (3/16) and 12.5% (2/16) of cases, respectively. Intra-subject differences between the branching patterns of lateral sides were observed in 37.50% (3/8) of cadavers.

Figure 32

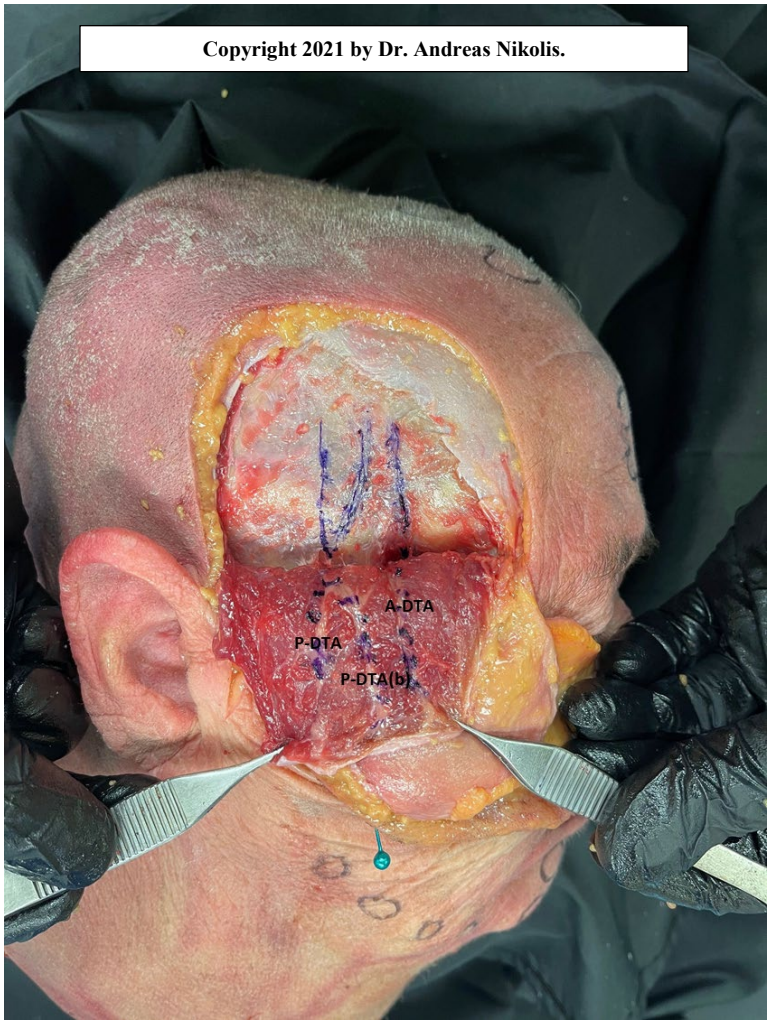
Bifurcations in the Anterior Deep Temporal Artery



Note: The anterior DTA (A-DTA) displayed bifurcations [A-DTA(b)] in 18.75% (3/16) of samples. In all observed cases, the DTAs were located under the temporalis muscle, superior to the periosteum. Markings in blue display where the DTAs would have laid, above the periosteum, prior to dissection. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

Figure 33

Bifurcations in the Posterior Deep Temporal Artery

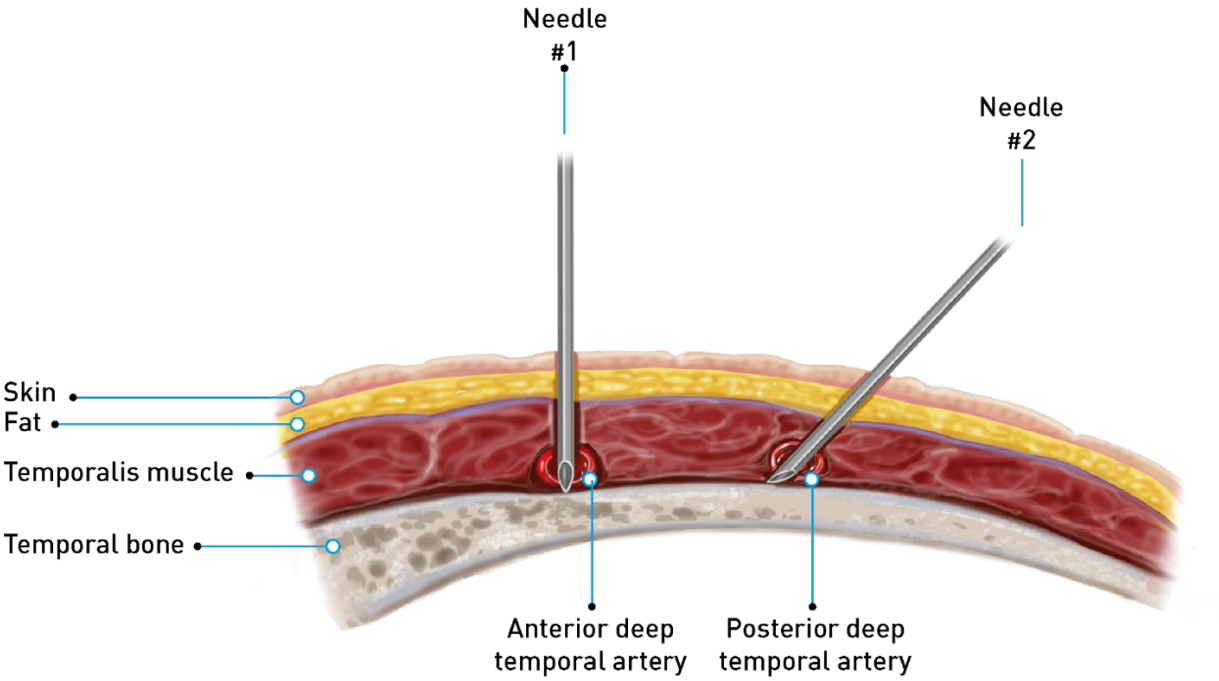


Note: The posterior DTA (P-DTA) displayed bifurcations [P-DTA(b)] in 12.5% (2/16) of samples. In all observed cases, the DTAs were located deep in the temporalis muscle, superior to the periosteum. Markings in blue display where the DTAs would have laid, above the periosteum, prior to dissection. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

Along with the superficial and middle temporal arteries, the DTAs are terminal branches of the internal and external carotid artery system. The DTAs various anastomoses with nearby arteries (e.g., the STA from the external carotid artery, the supraorbital artery from the ophthalmic artery) creates potential embolic pathways when intravascular injections occur, which can result in serious AEs. In the present study, as the DTAs were observed to be located at the deepest layer of the temporalis muscle, but superficial to the periosteum, it is possible for injectors to accidentally inject them, even while making needle contact with the bony cranium. This risk can be explained given the shape and size of the bevel of the needle barrel and the depth at which the DTAs are found (Figure 34). Given that the bevel may still cross the diameter of the DTAs while injecting on bone, the DTAs are subject to intravascular injection when performing aesthetic treatments with fillers. Furthermore, changes previously described (see section entitled “Gender effects of temporal hollowing”) now provide credence to the fact that the anatomy of the region changes based on age and gender.

Figure 34

Depth of the Deep Temporal Arteries



Note: The deep temporal arteries are subject to intravascular injection when performing aesthetic treatments with fillers, even while injecting deep. This risk can be explained by the shape and size of the bevel of the needle barrel and the depth at which the deep temporal arteries are found. The deep temporal arteries are located at the deepest layer of the temporalis muscle, but superficial to the periosteum. Therefore, it is possible for the bevel to cross the diameter of the arteries while making needle contact with the bony cranium, possibly leading to accidental intravascular injection. From “Topography of the Deep Temporal Arteries and Implications for Performing Safe Aesthetic Injections.” by Nikolis, Enright, Troupis et al., 2021.

Unlike the STA, which is often visible and palpable,[31] avoiding the DTAs during injections is more difficult for two principle reasons: 1) paucity of cadaveric dissections evaluating their location, and 2) the topography of the DTAs are unpredictable in comparison to other major temporal arteries. For example, one study reported that the STA was located 1cm anterior and 1cm superior from the apex of the tragus in 100% of cases.[200] However, in the present study we observed greater variability in the distance between the DTAs and standard anatomical landmarks. For example, D1 ranged from 0.8cm to 2.7cm; D2 ranged from 1.8cm to 4.2cm; D3 ranged from 0.3cm to 2.6cm; and D4 ranged from 1.5cm to 3.3cm (Table 2). Moreover, we observed three patterns of branching, including the classical branching pattern of the stem into separate anterior and posterior branches, as well as major bifurcations in the anterior and posterior branches. The variability in the location of the DTAs within the temporal fossa, as well as their inconsistent branching patterns among and within patients, impede the ability to classify a safe zone of injection.

When filler emboli lead to obstruction of the orbital or ophthalmic arteries, the resulting AEs are often irreversible, with little to no improvement in vision.[201,202] Therefore, it is vital for the trained professional to first attempt to prevent these AEs from occurring and then be prepared to recognize and manage any complications immediately. Controllable factors for injectors are the amount, speed, and pressure of injection. Small aliquots of filler should be injected slowly and gently, so that there will be an insufficient amount of product propelled into a vessel in the case of accidental intravascular injection.[47] When performing deep injections with small volumes at slow velocity and low pressure, any product placed intravascularly will reflux distally to small end vessels and

AEs will be limited (e.g., mild pain, tenderness, delayed bruising). As a precautionary measure, all aesthetic practitioners should have emergency treatment kits on hand.[203] The Aesthetic Complications Expert (ACE) Group recommends that kits include, among other items, hyaluronidase, acetylsalicylic acid and topical nitroglycerin.[204]

A recent national survey among ocular specialists revealed that, although 85% of respondents were aware of visual loss as a complication from fillers, the majority of practitioners (88%) did not have local management guidelines for vascular complications, nor were they aware of current management guidelines (75%). The authors concluded that according to the results of their survey, many clinicians do not have the appropriate experience to manage visual AEs associated with fillers. Subsequently, the treatment for visual disturbances are heterogeneous,[205] and patient outcomes have historically been poor. As others have suggested,[205] the development of specialist private referral networks for the emergency management of AEs may be warranted.

With sixteen unilateral assessments, our sample size is similar to other anatomical studies investigating the vascular anatomy of the temporal region.[37,195,196,199] However, a larger sample size with specific demographic variability (gender, ethnicity, age) may reveal significant effects of certain variables.[206] Further clinical evaluations are required to validate treatment techniques for rejuvenating the temporal region. The present literature search revealed the scarcity of studies conducted in living subjects, which relate the anatomy of the DTAs to the safety of injectable treatments (n = 1). However, the results of over forty years (1980-2021) of cadaveric research provide evidence of multiple pathways through which the DTAs could be involved in vascular AEs. Therefore, to

reduce the risk of AEs, injectors should take into consideration the topography of the DTAs, among other important vascular structures of the temporal region.

Conclusions

Our current findings support the concept that the development of temporal hollows is partly attributed to age-related structural changes. Notably, a lateral increase of the skull has been shown to occur with age in both genders, contributing to a prominence in bony facial features of the lateral aspect of the skull, such as the lateral orbital rims, temporal crests, and zygomatic arches. Additionally, a change in calvarial volume has been demonstrated in both males and females of advancing age, which has also been associated with soft tissue laxity. Such changes may promote the appearance of a skeletonized face and soft tissue reduction in older people. In particular, post-menopausal women tend to experience a significant reduction in temporal soft tissue volume, in comparison to their male counterparts. This likely is a contributing factor to the over-representation of women seeking treatment for temporal hollows.

The use of soft tissue fillers for temporal volumizing has become common practice within the past decade, with clinical data demonstrating an acceptable safety and efficacy profile.[6] Supraperiosteal placement of a bolus injection with a needle has been more frequently suggested for injecting into the temporal region, in order to avoid superficial temporal arterial branches.[207] The temporal fossa has demonstrated thinner soft tissue in its more cranial locations, such as near the temporal crest, suggesting cranial product placement to result in better restoration of temporal volume with less product used. Clinical results have also shown reduced thickness of soft tissue covering the filler product

when injected into cranial locations of the temporal fossa. Thus, the use of supraperiosteal injections may be recommended when there is less temporal soft tissue present. Injecting with supraperiosteal placement into the superior temple may also serve as a superior point of access for minimally invasive temporal augmentation procedures. Previous cross-sectional CT-imaging analyses revealed a significantly deeper temporal fossa to be present in males when compared to females. When utilizing a deep, supraperiosteal injection technique for the temporal region, injectors may consider using a longer needle in males than used in females. By doing so, bony contact will be made, allowing the product to be placed on the periosteum. However, it is important to note that injections making contact with bone can cause greater damage and deformity to the needle tip than those performed in soft tissues.[208] In order to mitigate the degree of damage, the number of injection passes should be minimized or, alternatively, the needle should be changed regularly. Aspiration is also recommended when injecting at the level of the bone.[207] Based on anatomical data, targeting the inter-fascial layers of the temporal region during soft tissue filler augmentation procedures poses the greatest risk.[161] Should this layer be targeted in treatment, the use of US-guided technology is recommended to identify vascular structures and confirm the proper positioning of the needle/cannula into the correct plane.

Despite the strong safety profiles of injectable products, various AEs have been associated with temporal augmentation procedures due to the complex vascular nature of the region. The potential anatomic variations of the major temporal arteries (i.e., STA, MTA, ZOA and DTAs) are aberrant, with ramifications of their subsidiary branches being complicated and vast. Therefore, the possibility for iatrogenic vascular damage during

various medical interventions, such as injection-based aesthetic treatments, is always a risk. Many of the proposed injection techniques are founded on empirical data rather than scientific evidence. Various authors have attempted to define a safe zone for injecting the temporal fossa and may have provided readers with a false sense of security, especially considering the findings from the two studies presented herein (e.g., i) validated gender differences in temporal anatomy; and ii) the vasculature of the DTAs). As minimally invasive techniques such as aesthetic injections are *blinded* procedures,[209] they cannot be performed with *definite* identification of all vascular structures.[28] A review of the literature including anatomical studies, clinical trials and AE case reports confirms there is no true "safe" zone devoid of risk to intra-vascular structures. The inability to see deep structures during filler injections is an inherent risk factor for AEs, even when an injector possesses an adequate knowledge of the surface anatomy and important landmarks. This inherent risk can be minimized and should not preclude seeking advanced training or treating the temporal fossa where indicated. Instead, it should be considered standard practice for injectors to follow risk-reducing procedures (e.g., identifying intra-arterial needle placement through aspiration, palpation, or US-guidance) and counsel patients on the inherent risks of the associated procedures, to make an informed decision. Even when implementing multiple preventative measures, injectors should know how to identify signs of an AE and methods of managing and treating filler-related AEs, which is not always the case.[205] Advanced knowledge on the temporal region vasculature is critical to minimize the risk of intravascular injection and subsequent devastating vascular complications such as arterial occlusion, ischemia or embolism. Our description of bony

changes and the position of the DTAs, as well as their possible role in AE development should lead to increased vigilance when performing filler treatments in the temporal area.

Summary of key findings

1. The bony temporal fossa does change with age, these changes are further impacted by significant soft tissue resorption over time and specifically by gender.
2. The position of the anterior and posterior DTAs have been identified in a cadaveric model and measured against easily palpable bony landmarks
3. Errors in the literature previously identifying the mechanism of action leading to blindness have been incorrectly attributed to vessels other than the causative DTAs.

Future directions

The present collection of work provide direction for future investigations, these include:

1. Developing treatment algorithms founded on the established changes to the temporal fossa stratified by age, gender, and all major superficial and deep vessels of the region.
2. Conduct a clinical trial(s) to validate the proposed treatment algorithm(s).
3. Re-evaluate all previously published cases of blindness in the literature associated with the temporal fossa region, to determine the possible role of the DTAs in AEs.
4. Expand dissections to other population of cadavers (by age and gender).
5. Angiographic evidence of DTAs position stratified by age and gender.

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