Aus der Klinik für Hand-, Plastische und Ästhetische Chirurgie
Klinikum der Ludwig-Maximilians-Universität München

Multimodale Untersuchung der fazialen Gefäßtopographie in der Frontal- und Perioralregion

Dissertation
zum Erwerb des Doktorgrades der Medizin
an der Medizinischen Fakultät der
Ludwig-Maximilians-Universität München

vorgelegt von
Michael Georg Alfertshofer

aus
Fürstenfeldbruck

Jahr
2023

Mit Genehmigung der Medizinischen Fakultät der
Ludwig-Maximilians-Universität zu München

Erster Gutachter:	Prof. Dr. med. Thilo Ludwig Schenck
Zweiter Gutachter:	Prof. Dr. med. Riccardo Giunta
Dritter Gutachter:	Prof. Dr. med. Carl-Peter Cornelius
ggf. weitere Gutachter:	
Mitbetreuung durch den promovierten Mitarbeiter:	Dr. med. Dr. med. univ. Konstantin Frank
Dekan:	Prof. Dr. med. Thomas Gudermann
Tag der mündlichen Prüfung:	31.07.2023

Affidavit

LMU
LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN
Promotionsbüro Medizinische Fakultät
MMRS

Eidesstattliche Versicherung

Alfertshofer, Michael Georg

Name, Vorname

Ich erkläre hiermit an Eides statt, dass ich die vorliegende Dissertation mit dem Titel:

Multimodale Untersuchung der fazialen Gefäßtopographie
in der Frontal- und Perioralregion

selbständig verfasst, mich außer der angegebenen keiner weiteren Hilfsmittel bedient und alle Erkenntnisse, die aus dem Schrifttum ganz oder annähernd übernommen sind, als solche kenntlich gemacht und nach ihrer Herkunft unter Bezeichnung der Fundstelle einzeln nachgewiesen habe.

Ich erkläre des Weiteren, dass die hier vorgelegte Dissertation nicht in gleicher oder in ähnlicher Form bei einer anderen Stelle zur Erlangung eines akademischen Grades eingereicht wurde.

München, 02. August 2023 Michael Alfertshofer

Inhaltsverzeichnis

Inhaltsverzeichnis

Abkürzungsverzeichnis

A…………………...Arteria
Aa……………….…Arteriae
M………………...Musculus
Mm……………...Musculi

Publikationsliste

I. Cotofana S MD PhD PhD, **Alfertshofer M**, Schenck T MD PhD, Bertucci V MD, Belezany K MD, Asher B MD, Lachman N MD PhD, Green JB MD, Swift A MD, Frank K MD. „Anatomy of the Superior and Inferior Labial Arteries revised: An Ultrasound Investigation and Implication for Lip Volumization“. Aesthetic Surgery Journal, May 2020. Doi: 10.1093/asj/sjaa137

II. Cotofana S MD PhD PhD, **Alfertshofer M**, Frank K MD, Bertucci V MD, Belezany K MD, Nikolis A MD, Sykes J MD, Swift A MD, Lachman N MD PhD, Schenck T MD PhD. „Relationship Between Vertical Glabellar Lines and the Supratrochlear and Supraorbital Arteries“. Aesthetic Surgery Journal, June 2020. Doi: 10.1093/asj/sjaa138

III. **Alfertshofer M**, Frank K MD, Melnikov D MD PhD, Möllhoff N MD, Gotkin R MD, Freytag D, Heisinger S MD, Giunta R MD PhD, Schenck T MD PhD, Cotofana S MD PhD PhD. “Performing Distance Measurements in Curved Facial Regions – A Comparison between 3D Surface Scanning and Ultrasound imaging”. Facial Plastic Surgery, March 2021. Doi: 10.1055/s-0041-1725166

Persönlicher Beitrag zu den Veröffentlichungen

1.1 Beitrag zu "Anatomy of the Superior and Inferior Labial Arteries revised: An Ultrasound Investigation and Implication for Lip Volumization" (Veröffentlichung I)

Der Doktorand, Herr Michael Georg Alfertshofer, hat im Rahmen der Co-Autorenschaft bei der Publikation „Anatomy of the Superior and Inferior Labial Arteries revised: An Ultrasound Investigation and Implication for Lip Volumization", welche im *Aesthetic Surgery Journal* im Mai 2020 publiziert wurde, das Thema der Publikation sowie den Studienaufbau gemeinsam mit Herrn Prof. Dr. med. Thilo Ludwig Schenck, Prof. Dr. med. Sebastian Cotofana und Dr. med. Dr. med. univ. Konstantin Frank entwickelt.

Hierbei fielen bei den Vorbereitungen die Erstellung des Studienprotokolls, die Erstellung von Probandeninformations- und Einwilligungsbögen, das Erlernen der Methoden, die Konzeption des Untersuchungsalgorithmus sowie die Akquise von ProbandInnen für diese Studie in seinen Aufgabenbereich. Die Durchführung der Studie sowie die Datenerfassung anhand der gesuchten primären und sekundären Studienziele in der Perioralregion wurde anhand objektiver Messmethoden eigenständig und alleinig durch den Doktoranden Michael Georg Alfertshofer durchgeführt. Die Auswertung und die statische Analyse der erhobenen Messdaten, die Erstellung des Publikationsmanuskripts sowie das Anfertigen der Abbildungen und Illustrationen für das Manuskript erfolgten in Zusammenarbeit mit Prof. Dr. med. Thilo Schenck, Prof. Dr. med. Sebastian Cotofana und Dr. med. Dr. med. univ. Konstantin Frank.

1.2 Beitrag zu “Relationship Between Vertical Glabellar Lines and the Supratrochlear and Supraorbital Arteries“ (Veröffentlichung II)

Der Doktorand, Herr Michael Georg Alfertshofer, hat im Rahmen der Co-Autorenschaft bei der Publikation „Relationship Between Vertical Glabellar Lines and the Supratrochlear and Supraorbital Arteries“, welche im *Aesthetic Surgery Journal* im Juni 2020 publiziert wurde, das Thema der Publikation sowie den Studienaufbau gemeinsam mit Herrn Prof. Dr. med. Thilo Ludwig Schenck und Prof. Dr. med. Sebastian Cotofana und Dr. med. Dr. med. univ. Konstantin Frank entwickelt.

Hierbei fielen bei den Vorbereitungen die Erstellung des Studienprotokolls, die Erstellung von Probandeninformations- und einwilligungsbögen, das Erlernen der Methoden, die Konzeption des Untersuchungsalgorithmus sowie die Akquise von ProbandInnen für diese Studie in seinen Aufgabenbereich. Die Durchführung der Studie sowie die Datenerfassung anhand der gesuchten primären und sekundären Studienziele in der Frontalregion wurde anhand objektiver Messmethoden eigenständig und alleinig durch den Doktoranden Michael Georg Alfertshofer durchgeführt. Die Auswertung und die statistische Analyse der erhobenen Messdaten, die Erstellung des Publikationsmanuskripts sowie das Anfertigen der Abbildungen und Illustrationen für das Manuskript erfolgten erfolgten in Zusammenarbeit mit Prof. Dr. med. Thilo Schenck, Prof. Dr. med. Sebastian Cotofana und Dr. med. Dr. med. univ. Konstantin Frank.

1.3 Beitrag zu „Performing Distance Measurements in Curved Facial Regions – A Comparison between 3D Surface Scanning and Ultrasound Imaging” (Veröffentlichung III)

Der Doktorand, Herr Michael Georg Alfertshofer, hat im Rahmen der Erst-Autorenschaft bei der Publikation "Performing Distance Measurements in Curved Facial Regions – A Comparison between 3D Surface Scanning and Ultrasound Imaging", welche im März 2021 in *Facial Plastic Surgery* publiziert wurde, das Studiendesign zunächst eigenständig entwickelt und mit Herrn Prof. Dr. med. Thilo Schenck und Prof. Dr. med. Sebastian Cotofana weiter verbessert. Hierbei wurden Studienmethoden entwickelt, welche die hier vorgestellten Messmethoden des 3D-Oberflächen-Scans und der Ultraschall-Distanz-Messung objektiv miteinander vergleichen können. Die Vorbereitungen wie die Entwicklung der Studienidee, die Erstellung eines Studienprotokolls und die Erstellung von Probandeninformations- und einwilligungsbögen erfolgten selbstständig. Die Durchführung der Studie sowie die Datenerfassung wurde anhand der objektiven Messmethoden eigenständig und alleinig durch den Doktoranden Michael Georg Alfertshofer durchgeführt. Die Auswertung und die statistische Analyse der erhobenen Messdaten, die Erstellung des Publikationsmanuskripts sowie das Anfertigen der Abbildungen und Illustrationen für das Manuskript erfolgten zunächst eigenständig. Anschließend wurden diese bei Bedarf durch Prof. Dr. med. Thilo Schenck und Prof. Dr. med. Sebastian Cotofana korrigiert und schließlich in eigenständiger Arbeit in ihre finalen Fassungen gebracht.

2. Einleitung

2.1 Plastisch-ästhetische Eingriffe im Gesicht

Laut der jährlichen Statistik der International Society of Aesthetic Plastic Surgery (ISAPS) wurden im Jahr 2019 weltweit 4.058.143 plastisch-ästhetische Operationen in der Gesichts- und Kopfregion durchgeführt. Dies entspricht einem Anstieg von circa 14% gegenüber dem Vorjahr, in welchem eine Anzahl von 3.574.408 Operationen berichtet wurde.[1] Somit stellt die Gesichts- und Kopfregion die Körperregion dar, in welcher die meisten plastisch-ästhetischen Operationen durchgeführt werden. Diese hohe Nachfrage nach Operationen, welche unter anderem der Verjüngung des Gesichts sowie der ästhetischen Verbesserung bestimmter Gesichtsareale dienen, spiegelt die Bedeutung der Gesichts- und Kopfregion für die ästhetische Wahrnehmung wider.[2,3]

Aufgrund der Tatsache, dass Operationen jedoch zeit- und kostenintensiv sind sowie ein größeres Risiko für peri- und postoperative Komplikationen aufweisen, entwickelten sich in den letzten Jahrzehnten zunehmend effektive minimal-invasive Alternativen.[4–6] Die Nachfrage nach minimal-invasiven Eingriffen, die ebenso der Minimierung von Alterserscheinungen und der ästhetischen Verbesserung des Gesichts dienen, stieg in den letzten Jahren analog zu den operativen plastisch-ästhetischen Eingriffen stark an: So konnte ein Zuwachs von 225% in der Anzahl der durchgeführten minimal-invasiven ästhetischen Eingriffen des Gesichts im Jahr 2019 verglichen zum Jahr 2000 in der US-amerikanischen Bevölkerung festgestellt werden.[7] Das Repertoire an minimal-invasiven ästhetischen Eingriffen ist groß und wächst mit zunehmender Weiterentwicklung der Produkte und Behandlungstechniken durch stärkeren wissenschaftlichen Austausch beständig.[4–6,8–10]

Einen signifikanten Anteil an diesen minimal-invasiven ästhetischen Eingriffen stellen hierbei Injektionen mit Soft-Tissue-Filler dar: Diese Art des minimal-invasiven ästhetischen Eingriffs wurde im Jahr 2019 knapp 2,7 Millionen Mal in den USA durchgeführt.[7]

Mithilfe von präzise gesetzten Boli von Soft-Tissue-Filler kann Volumen dosiert in verschiedenen Regionen des Gesichts den ästhetischen Wünschen entsprechend appliziert werden. Die Anwendungsmöglichkeiten sind hierbei vielfältig und reichen von der Minimierung von typischen Alterserscheinungen wie Hautfalten über die Akzentuierung bestimmter Gesichtsregionen (zum Beispiel Volumisierung der Lippen) bis hin zur Reduktion von krankheitsbedingten Stigmata wie der Lipatrophie des Mittelgesichts bei HIV-Patienten.[11–14] Laut der jährlichen Statistik der American Society of Plastic Surgeons (ASPS) stellt Hyaluronsäure mit knapp 80% von allen durchgeführten Soft-Tissue-Filler-Injektionen (insgesamt 2.721.469) das am häufigsten verwendete Soft-Tissue-Filler-Material in der US-Bevölkerung im Jahr 2019 dar.[7] Hyaluronsäure ist ein körpereigenes Glykosaminoglykan, welches für den Aufbau und Erhalt des Bindegewebes essentiell ist. Folglich kommt dem Hyaluronsäure-Gehalt der Haut eine entscheidende Bedeutung bei der Entwicklung von typischen Alterserscheinungen der Haut zu.[15–17]

2.2 Komplikationen minimal-invasiver Eingriffe im Gesicht

Trotz der minimal-invasiven Natur dieser Eingriffe können dennoch Komplikationen während und nach Soft-Tissue-Filler-Injektionen auftreten. Allgemeine Komplikationen umfassen beispielsweise Schmerzen, Schwellungen und Hämatome und sind typischerweise durch die Penetration der Nadel durch die Haut bedingt.[18,19] Neben allgemeinen Komplikationen wurden allerdings in seltenen Fällen auch schwerwiegendere Folgen nach Injektionen mit Soft-Tissue-Filler beschrieben: Beleznay et al. berichteten in zwei systematischen Reviews aus den Jahren 2015 und 2019, dass weltweit bis dato 146 Fälle von Erblindungen in Zusammenhang mit Soft-Tissue-Filler-Injektionen im Gesicht beschrieben wurden.[20,21] Die Frontal- und Glabellaregion stellten hierbei mit 48,6% der Fälle (insgesamt 72 Fälle) die Gesichtsregionen dar, in welchen die meisten Erblindungen nach zuvor durchgeführten Soft-Tissue-Filler-Injektionen auftraten.[20,21] Typische Gründe für Soft-Tissue-Filler-Injektionen in diesem Bereich sind die Reduktion von Zornesfalten in der Glabellaregion sowie die Reduktion von horizontalen Stirnfalten in der Frontalregion.

Die dominanten Arterien in der Frontal- und Glabellaregion sind die Arteria (A.) supratrochlearis medial und die A. supraorbitalis lateral.[22] Beide Arterien entspringen der A. ophthalmica. Die A. ophthalmica gibt weiterhin die A. centralis retinae als versorgende Arterie des Auges ab.[23] Nach aktuellem Kenntnisstand wird davon ausgegangen, dass im Falle der beschriebenen Erblindungen nach Soft-Tissue-Filler-Injektionen akzidentiell ein Bolus von Soft-Tissue-Filler in die A. supratrochlearis oder A. supraorbitalis injiziert wird. Es wird vermutet, dass der injizierte Bolus bei ausreichendem Injektionsdruck retrograd der Flußrichtung des Blutes zur A. ophthalmica wandert und so kleinere Gefäßäste der A. centralis retinae okkludieren kann. Aus dieser Okklusion folgt eine nachfolgende Minderperfusion und schlussendlich eine Ischämie der retinalen Zellen des Auges mit resultierendem Visusverlust.[24–27]

Abhängig von der okkludierten Arterie und dem damit versorgten Gewebe können unterschiedliche Folgen auftreten: So können eine weitere Folge von Gefäßokklusionen nach Soft-Tissue-Filler-Injektionen auch Nekrosen der Gesichtshaut sein, welche beispielsweise in der Nasal-, Bukkal- und Perioralregion nach Volumenaugmentationen der Lippen auftreten können. Analog werden in solchen Fällen kleinere anastomosierende Hautäste durch Soft-Tissue-Filler-Material, welches zuvor vermutlich akzidentiell in die A. labialis superior oder A. labialis inferior im Falle von Lippenaugmentationen injiziert wurde, okkludiert.[28–30] Weiterhin wurden auch bereits Fälle von Schlaganfällen nach Injektionen von Soft-Tissue-Filler im Gesicht beschrieben.[31,32]

Dieses Krankheitsbild und der dahinter vermutete Pathomechanismus, welcher sich in verschiedenen klinischen Bildern äußern kann, ist auch unter dem Namen *Embolia cutis medicamentosa* (Nicolau-Syndrom) bekannt und beschreibt im Allgemeinen die Okklusion einer Arterie durch ein injiziertes Medizinprodukt.[33,34] Durch die zahlreichen arteriellen Gefäßanastomosen des Gesichts können Komplikationen auch an einer anderen Stelle als der ursprünglich behandelten Gesichtsregion auftreten, da der versehentlich intravasal applizierte Bolus entlang dieser Anastomosen bei ausreichendem Injektionsdruck verschleppt werden kann.[35–37]

2.3 Minimierung von Komplikationen durch anatomisch-deskriptive Studien

Da es sich bei Soft-Tissue-Filler-Injektionen um elektive Eingriffe handelt, muss ganz besonders auf ein günstiges Nutzen-Risiko-Verhältnis mit höchstmöglicher Patientensicherheit und gleichzeitig bestmöglichem ästhetischem Ergebnis geachtet werden. Um derartig schwerwiegende Komplikationen wie Hautnekrosen, Visusverlust und ischämische Schlaganfälle zu verhindern, ist ein fundiertes Wissen und Verständnis über die topographische Anatomie, Variationen sowie die Verteilung von Arterien im Gesicht essentiell.[38,39]

Auf Grundlage von zuvor durchgeführten anatomisch-deskriptiven Studien wurde so versucht, Handlungsempfehlungen für sichere und effektive Soft-Tissue-Filler-Injektionen abzuleiten.[40–49]

Ein besonderer Fokus lag in diesen Untersuchungen auf der Frontal- und Perioralregion. Die Frontal- und Glabellaregion im oberen Gesichtsdrittel sowie die Perioralregion im unteren Gesichtsdrittel sind für den mimischen Ausdruck von Emotionen und somit für die menschliche Kommunikation essentiell.[50–52] Aus diesem Grund kommt diesen Gesichtsregionen auch eine gesteigerte Aufmerksamkeit bei persönlicher Interaktion zu, weshalb Soft-Tissue-Filler-Injektionen zur ästhetischen Verbesserung dieser Gesichtspartien hier besonders relevant sind und folglich häufig durchgeführt werden.

2.3.1 Bisheriger Forschungsstand: Frontalregion

Um die anatomisch-topographischen Verhältnisse der Gefäße in der Frontalregion zu untersuchen, wurden zahlreiche Studien durchgeführt. Die wichtigsten Publikationen sind im Folgenden aufgeführt:

Im Jahr 2000 untersuchten Vural et al. die topographische Beziehung der vertikalen Glabellafalten und der A. supratrochlearis in der Dissektion von Körperspendern (n = 8) sowie der Ultraschalluntersuchung von freiwilligen Studienteilnehmern (n = 19). In 59% der Fälle war das supratrochleare Gefäßbündel an der vertikalen Glabellafalte lokalisiert, während in den restlichen 41% der Verlauf nicht weiter als 3,2 mm lateral der Glabellafalte lokalisierbar war. Als Folge hieraus wurde postuliert, dass die vertikale Glabellafalte einen verlässlichen Orientierungspunkt für die A. supratrochlearis darstellt.[40] Ugur et al. untersuchten in einer Studie aus dem Jahr 2008, ob der mediale Kanthus einen verlässlichen Orientierungspunkt für das supratrochleare Gefäßbündel darstellt, da die Autoren klinisch die Erfahrung gemacht haben, dass die A. supratrochlearis häufig deutlich weiter lateral verläuft als von Vural et al. beschrieben. Hierbei wurden Studienteilnehmer mit Ultraschall (n = 57) und weiterhin Körperspender mittels Dissektion (n = 15) untersucht. Dieses Gefäßbündel verlief maximal 3mm lateral oder medial des medialen Kanthus mit einer durchschnittlichen Distanz von 0,8 ± 0,7 mm. Die durchschnittliche Distanz zur vertikalen Glabellafalten wurde mit 6,2 ± 1,7 mm angegeben.[41] In einer Ultraschall-Studie (n = 50) von Hyun et al. aus dem Jahr 2020 wurde der Verlauf von Blutgefäßen der Frontalregion in Bezug auf die Mittellinie untersucht. Untersucht wurde, ob Blutgefäße innerhalb eines Korridors von 1,5 cm um die Mittellinie der Frontalregion (0,75 cm lateral auf beiden Seiten) verlaufen. Dieser Korridor wurde in vier horizontale Rechtecke unterteilt. (P4 am kaudalsten, P3, P2 und P1 am kranialsten) In der P4-Region, welche die relevanteste Region für Soft-Tissue-

Filler-Injektionstherapien darstellt, konnten in 3,3% der Fälle Arterien identifiziert werden. Die horizontale Distanz von der Mittellinie in dieser Region lag bei 5,50 mm.[42]

2.3.2 Bisheriger Forschungsstand: Perioralregion

Um die anatomisch-topographischen Verhältnisse der Gefäße in der Perioralregion zu untersuchen, wurden zahlreiche Studien durchgeführt. Die wichtigsten Publikationen sind im Folgenden aufgeführt:

Eine Studie von Cotofana et al. aus dem Jahr 2017 untersuchte das Verteilungsmuster der Aa. labiales superior et inferior in Bezug auf die Gewebeschicht, innerhalb welcher diese verlaufen. Hierbei wurden drei Schichten unterschieden: Die submuköse Schicht zeigte die Arterien am häufigsten in 78,1%, die intramuskuläre Schicht in 17,5% und die subkutane Schicht in 2,1% der Fälle.[44] Vergleichbare Werte wurden trotz unterschiedlicher Nomenklatur in einer Studie von Lee et al. aus dem Jahre 2019 angegeben.[53] In einer Studie von Tansatit et al. aus dem Jahr 2014, in welcher n = 26 Körperspender (13 männlich, 13 weiblich) untersucht wurden, zeigte die A. labialis superior einen durchschnittlichen Gefäßdurchmesser von 1,1 ± 0,3 mm und eine durchschnittlichen Tiefe zur Hautoberfläche von 4,5 ± 0,8 mm. Die A. labialis inferior zeigte einen durchschnittlichen Gefäßdurchmesser von 1,3 ± 0,2 mm und eine durchschnittliche Tiefe von 4,7 ± 1,1 mm.[54] Neben dem Durchmesser und der Tiefe untersuchte eine Studie von Money et al. aus dem Jahr 2019 die Distanz der A. labialis superior zur Lippenrot-Haut-Grenze an 18 Körperspendern. Mithilfe eines Messschiebers wurden an den Messpunkten P1-P4 folgende Distanzen von lateral (P1, am Mundwinkel) nach medial (P4, in der Mittellinie) gemessen: P1 mit 8,48 ± 1,71 mm, P2 mit 2,04 ± 2,52 mm, P3 mit 1,03 ± 3,02 mm und P4 mit 1,80 ± 2,74 mm jeweils kranial der Lippenrot-Haut-Grenze. Entgegen der vorhergehenden Studien wurde allerdings eine andere Verteilung in Bezug auf die Schichten der Lippen gemessen: In 85-92% verlief die A. labialis superior hier submukosal.[46]

2.4 Fragestellung, Hypothesen und Zielsetzung

Die bisher durchgeführten Studien zur arteriellen Topographie in der Frontal- und Perioralregion fokussierten sich lediglich auf einzelne Komponenten in der komplexen drei-dimensionalen Topographie der Arterien. Diese erlaubten somit kein drei-dimensionales und somit vollständiges Bild über den topographischen Verlauf der Arterien. Zusätzlich wurden in einigen der bisher durchgeführten Studien die Ergebnisse, welche mittels Dissektion von Körperspendern und apparativen in-vivo-Untersuchungen von Studienteilnehmern gewonnen wurden, undifferenziert miteinander kombiniert. Aufgrund möglicher Fixierungs-bedingter Veränderungen der anatomisch-topographischen Verhältnisse, weisen Studien, welche auf der Dissektion von Körperspendern basieren, Limitationen in der Anwendbarkeit auf die Anatomie des Lebenden auf. Zusätzlich sind andere ethnische Studienpopulationen nur bedingt auf die kaukasische Bevölkerung anwendbar.

Die ganzheitliche drei-dimensionale Untersuchung der topographischen Verhältnisse der Arterien in der Frontal- und Perioralregion in Bezug auf kutane Landmarken des Gesichts sind daher Untersuchungsobjekt dieser Dissertation, um individualisierte Untersuchungen und darauf basierende Soft-Tissue-Filler-Injektionen zu ermöglichen. In dieser Dissertation wird weiterhin ein standardisierter Untersuchungsalgorithmus für die individuelle Evaluation der topographischen Gefäßverhältnisse im Gesicht des Patienten durch die Kombination von Ultraschall und 3D-Oberflächen-Scans vorgestellt.

2.4.1 Frontalregion

Im Rahmen dieser Dissertation soll die Hypothese, dass die A. supratrochlearis verlässlich in der vertikalen Glabellafalte verläuft und Injektionen lateral dieser Landmarke folglich als weitestgehend sicher anzusehen sind, überprüft werden. Weiterhin soll überprüft werden, ob die A. supratrochlearis allgemein in einem verlässlichen Abstand zu einer kutanen Landmarke (Mittellinie und vertikale Glabellafalte) verläuft. Dies lässt sich auch auf die A. supraorbitalis adaptieren, bei welcher ebenfalls untersucht wird, ob ein topographischer Verlauf im Sinne eines verlässlichen Abstands zur Mittellinie und zur ipsilateralen vertikalen Glabellafalte angenommen werden kann. Um ein genaues, drei-dimensionales Bild über den topographischen Verlauf zu erhalten, werden weiterhin folgende Parameter untersucht: Durchmesser, Tiefe, Abstand zur Mittellinie, Abstand zur vertikalen Glabellafalte und Verschieblichkeit bei Provokation der Glabellafalten, welche durch die Kontraktion der Musculi (Mm.) corrugatores supercilii entstehen. Mithilfe dieser Parameter kann ein Korridor für die A. supratrochlearis und supraorbitalis eruiert werden, in welchem die Arterien der Glabellaregion mit höchster Wahrscheinlichkeit, sowohl ohne wie auch mit mimischer Aktivität, verlaufen. Mit diesem Wissen können Effektivität und Sicherheit von Soft-Tissue-Filler-Injektionen in diesen Gesichtsregionen sowie die prä-operative Planung und peri-operative Durchführung von Operationen wie Rotationslappenplastiken beispielsweise für Nasenrekonstruktionen verbessert werden.[55–57]

2.4.2 Perioralregion

Im Rahmen dieser Dissertation soll weiterhin untersucht werden, ob die Aa. labiales superior et inferior in einem verlässlichen Abstand zur Lippenrot-Haut-Grenze verlaufen. Um ein drei-dimensionales Bild des topographischen Gefäßverlaufs zu erhalten, werden hier an sechs definierten Messpunkten (Drei Messpunkte an der Oberlippe P1-P3, Drei Messpunkte an der Unterlippe P4-P6) der Durchmesser, die Tiefe, der Abstand der Arterie zur Lippenrot-Haut-Grenze sowie die Schicht, in welcher die Arterien verlaufen, untersucht. Auf Grundlage der gewonnenen Erkenntnisse über die topographische Anatomie der Arterien können die Effektivität und Sicherheit von Soft-Tissue-Filler-Injektionen in der Perioralregion, beispielsweise bei Volumisierungen von Lippen sowie bei operativen Eingriffen in diesem Bereich, beispielsweise bei rekonstruktiven Lappenplastiken[58] verbessert werden.

2.4.3 Vorstellung eines Untersuchungsalgorithmus für individualisierte anatomisch-topographische Untersuchungen

Weiterhin wird im Rahmen dieser Dissertation ein bislang nicht beschriebener Untersuchungsalgorithmus für eine individualisierte Untersuchung der topographischen Gefäßanatomie im Gesicht vorgestellt. Dabei wird die Ultraschalluntersuchung mit farbkodierter Duplexsonographie zur Darstellung der Gefäße mit 3D-Oberflächen-Scans zur Referenzierung auf der Gesichtsoberfläche kombiniert. Diese Methoden können dabei mithilfe von Referenzpunktmarkierungen auf der Hautoberfläche miteinander korreliert werden, um so Untersuchungen „unter der Haut“ (Ultraschall) mit Untersuchungen „auf der Haut“ (3D-Oberflächen-Scans) miteinander kombinieren zu können. Mithilfe dieses Untersuchungsalgorithmus können Distanzen mithilfe von Ultraschall und 3D-Oberflächenscans zu zuvor markierten kutanen Orientierungspunkten auf der gesamten

Körperoberfläche gemessen und miteinander korreliert werden, was eine individualisierte Untersuchung der Anatomie – auch außerhalb der Gesichtsregion - erlaubt.

3. Zusammenfassung (Deutsch)

Hintergrund: In den letzten Jahren stieg die Nachfrage nach ästhetischen Soft-Tissue-Filler- Injektionen im Gesicht, insbesondere in der Frontal- und Perioralregion, stark an. Gleichzeitig stieg die Zahl an Komplikationen, die darauf zurückgeführt werden, dass Gefäße verletzt oder okkludiert werden. Nach aktuellem Kenntnisstand können Gefäßokklusionen durch akzidentielle Injektionen von Soft-Tissue-Filler in eine Arterie mit daraus resultierender Minderperfusion und Ischämie des nachfolgenden Gewebes entstehen. Dieses Phänomen ist auch unter dem Namen *Embolia cutis medicamentosa* (Nicolau-Syndrom) bekannt. Um die Rate an derartigen Komplikationen zu minimieren, wurden in den vergangenen Jahren zahlreiche anatomisch-deskriptive Studien über die topographischen Verhältnisse von Gefäßen in Gesichtsregionen, die besonders häufig von akzidentiellen Injektionen betroffen sind, durchgeführt. Genaue Kenntnis und ein profundes Verständnis über die topographischen Verläufe der Arterien des Gesichts ist unabdingbar, um Patientensicherheit und eine hohe Effektivität bei Soft-Tissue-Filler-Injektionen zu gewährleisten. Dieses Wissen kann weiterhin gewinnbringend bei rekonstruktiven Lappenplastiken im Gesicht eingesetzt werden.

Material und Methoden: An einem Probandenkollektiv von n = 41 Probanden (21 weiblich, 20 männlich) mit einem durchschnittlichen Alter von 26,17 ± 9,6 Jahren und einem durchschnittlichen Body Mass Index (BMI) von 23.09 ± 2.3 kg/m^2 wurde die Gefäßtopographie in der Frontal- und Perioralregion mithilfe von Ultraschall und photographischen 3D-Oberflächen-Scans untersucht. Die Messungen erfolgten dabei in Bezug zu kutanen Orientierungspunkten (Referenzpunkte) in der Frontalregion (Mittellinie und ipsilateral vertikale Glabellafalte) und in der Perioralregion (Lippenrot-Haut-Grenze). Die Orientierungspunkte wurden mithilfe von Steri-Strips™ (3M, Neuss, Germany) markiert.

Durch die Schallschatten, welche durch die Steri-Strips™ im Ultraschallbild erzeugt wurden, konnten die kutanen Referenzpunkte im Ultraschall-Bild sichtbar gemacht werden. Somit konnten die Gefäße, ihre Distanzen zu den Orientierungspunkten und der Hautoberfläche sowie ihre Durchmesser an definierten Messpunkten untersucht werden. In einer weitergehenden Untersuchung wurde die Kompatibilität und Kombinierbarkeit beider Methoden (Ultraschall und 3D-Oberflächen-Scans) untersucht. Dabei wurden Steri-Strips™ (3M, Neuss, Germany) mit einer definierten Länge von 20 mm in verschiedene Gesichtsregionen mit unterschiedlichen Wölbungen platziert, um die Länge mithilfe beider Methodiken vergleichend zu messen und Aussagen über die Korrelation beider Messmethoden mit dem Blick „von innen“ (Ultraschall) und „von außen“ (3D-Oberflächen-Scans) zu treffen.

Ergebnisse: In der Frontalregion verlief die A. supratrochlearis durchschnittlich 15,5 ± 3,5 mm und die A. supraorbitalis 27,8 ± 5,3 mm lateral der Mittellinie. In Bezug auf die vertikalen Glabellafalten verlief die A. supratrochlearis mit einer durchschnittlichen Distanz von 9,5 ± 3,4 mm und die A. supraorbitalis mit 21,7 ± 4,8 mm. Die durchschnittlichen Durchmesser betrugen 0,90 ± 0,02 mm für die A. supratrochlearis und 0,70 ± 0,02 mm für die A. supraorbitalis. Die durchschnittliche Distanz zur Hautoberfläche (= Tiefe der Arterie) betrug für die A. supratrochlearis 3,34 ± 0,6 mm und 3,54 ± 0,8 mm für die A. supraorbitalis. Bei Kontraktion des jeweiligen Musculus (M.) corrugator supercilii in der Glabellaregion (Provokation der Glabellafalten) bewegten sich die A. supratrochlearis um durchschnittlich 3,1 mm zur Mittellinie und 1,8 mm zur ipsilateralen vertikalen Glabellafalte nach medial. Die A. supraorbitalis bewegte sich hierbei um durchschnittlich 3,7 mm zur Mittellinie und um 2,3 mm zur ipsilateralen vertikalen Glabellafalte nach medial.

In der Perioralregion verliefen die A. labialis superior et inferior in 83,7% der Fälle (206 von 240 Messpunkten) innerhalb des Lippenrots. In den Messpunkten der Mittellinie (P2 in der Oberlippe und P5 in der Unterlippe) verliefen alle untersuchten Arterien innerhalb des Lippenrots. Die durchschnittliche Distanz der Aa. labiales superior et inferior zur Lippenrot-Hautgrenze betrug 1,8 ± 2,5 mm. Der durchschnittliche Gefäßdurchmesser der A. labialis superior betrug 0,91 ± 0,2 mm in den lateralen Messpunkten der Oberlippe (P1 und P3) und 0,75 ± 0,1 mm im medialen Messpunkt (P2) der Arterien, während dieser für die A. labialis inferior 0,83 ± 0,2 mm in den lateralen Messpunkten der Unterlippe (P4 und P6) und 0,76 ± 0,2 mm im medialen Messpunkt (P5) betrug. Die Arterien zeigten somit einen schmäler werdenden Gefäßdurchmesser im Verlauf nach medial. Der häufigste Verlaufstyp der Lippenarterien war der submukosale Verlauf in 58,5% der Fälle, gefolgt vom intramuskulären Verlauf (36,2%) und dem subkutanen Verlauf (5,3%). Die durchschnittliche Distanz zur Hautoberfläche (=Tiefe der Arterien) betrug 5,6 ± 1,3 mm für die A. labialis superior und 5,2 ± 1,4 mm für die A. labialis inferior.

Die durchschnittliche gemessene Länge des 20 mm - Steri-Strips^{TM} betrug 18,83 ± 0,08 mm [Range: 1,62 – 2,02 mm] in der Ultraschallmessung und 19,89 ± 0,02 mm [Range: 1,92 – 2,04 mm] in der 3D-Oberflächen-Scan-Messung, unabhängig von der Gesichtsregion mit $p < 0,0001$. Somit betrug die durchschnittliche Differenz zur standardisierten Länge (20 mm) der Referenzmarkierung 1,17 ± 0,3 mm bei der Ultraschallmessung und 0,11 ± 0,1 mm bei 3D-Oberflächen-Scan-Messungen. Die Differenz betrug somit 1,07 mm zwischen beiden Messmethoden. Die Ultraschallmessungen zeigte in der Frontalregion (als Beispiel einer „flacheren“ Gesichtsregion mit geringer Konkavität und Konvexität) genauere Messergebnisse mit einer Differenz von 0,59 mm (0,65 ± 0,4 mm in der Ultraschallmessung und 0,06 ± 0,2 mm in der 3D-Oberflächen-Scan-Messung), mit $p < 0,0001$ zwischen beiden Messmethoden.

Schlussfolgerung: Die zuvor postulierte Hypothese, dass die A. supratrochlearis in oder unmittelbar neben der Glabellafalte verläuft und somit Injektionen lateral der vertikalen Glabellafalten als sicher anzusehen sind, kann auf Grundlage der hier gewonnenen Daten verworfen werden. Die A. supratrochlearis zeigte in der Studie eine hohe Variabilität im Verlauf. Die große Variabilität zeigte sich auch im Falle der A. supraorbitalis, die in ihrer horizontalen Distanz zur Mittellinie und der vertikalen Glabellafalte große Unterschiede aufzeigte. Diese Variabilität macht Vorhersagen über den anatomisch-topographischen Verlauf der Arterien im Sinne eines verlässlichen Abstands zu Referenzpunkten nahezu unmöglich.

Es konnte gezeigt werden, dass die Aa. labiales superior et inferior in keinem einheitlichen Abstand zur Lippenrot-Haut-Grenze verlaufen. Auf Grundlage der hier gewonnenen Daten sind Injektionen in der Perioralregion außerhalb des Lippenrots als unbedenklicher im Vergleich zu den häufig praktizierten Injektionstechniken innerhalb des Lippenrots einzustufen, da die Aa. labiales superior et inferior dort mit niedrigerer Wahrscheinlichkeit verlaufen. Die Patientensicherheit sowie die Effektivität der Behandlung bei Soft-Tissue-Filler-Injektionen in der Frontal- und Perioralregion sowie die prä-operative Planung von gestielten Lappenplastiken im Gesichtsbereich kann mithilfe der hier gewonnenen Erkenntnisse über durchschnittliche topographische Verläufe der untersuchten Gefäße verbessert werden.

Weiterhin wurde hier ein standardisierter Untersuchungsalgorithmus für die individualisierte Analyse der anatomisch-topographischen Verhältnisse von Arterien vorgestellt. Die Distanzmessung via Ultraschall und 3D-Oberflächen-Scans wurden objektiv miteinander verglichen. So konnte gezeigt werden, dass Distanzmessungen im Ultraschallbild für die prä-operative Planung in flachen Gesichtsregionen (beispielsweise Frontalregion) gewinnbringend eingesetzt werden können. Die größte klinische Anwendbarkeit wird jedoch durch die Kombination aus beiden Methoden, Ultraschall und 3D-Oberflächen-

Scans, erreicht, da durch diese Kombination Strukturen „unter der Haut“ wie Gefäße in Bezug zu Strukturen „auf der Haut“ wie den Referenzpunkten gesetzt werden können.

4. Abstract (English)

Background: In recent years, the demand for aesthetic soft tissue filler injection therapies in the face, especially in the frontal and perioral region, has risen sharply. Concomitant with the increasing demand, the number of complications supposedly caused by vascular injury and occlusion increased. According to current knowledge, vascular occlusion is caused by an accidental injection of soft tissue fillers into an artery with reduced perfusion and ischemia of the anterograde tissue. This phenomenon is also known as *embolia cutis medicamentosa* (Nicolau-syndrome). The topographical anatomy of vessels in facial danger zones (such as the frontal and perioral region) were subject to a myriad of anatomic-descriptive studies. Precise knowledge of the topographical courses of facial arteries is essential to ensure patient safety and treatment efficacy. Furthermore, this knowledge can be helpful for reconstructive facial flap surgery.

Materials and methods: A group of n = 41 subjects (21 female, 20 male) with an average age of 26.17 ± 9.6 years and an average body mass index (BMI) of 23.09 ± 2.3 kg / m2 was analyzed with respect to the topography of arteries in the frontal and perioral region using ultrasound and photographic 3D-surface scans. The measurements were performed in relation to cutaneous orientation points (reference points) in the frontal region (midline and ipsilateral vertical glabellar line) and in the perioral region (vermilion border). The 3D surface scans were used to precisely position the reference points and to measure the dimensions of the respective regions of the face (e.g., width and length of forehead). These reference points were set with help of Steri-Strips™ (3M, Neuss, Germany). Due to the formation of sound shadows, the reference points were visible in the ultrasound image to visualize vessels, measure their distances to the reference points and the skin surface as well as their diameter at defined measurement points.

In order to test compatibility and combinability of both measurement methods, reference points, Steri-Strips™, with a defined length of 20 mm were placed in facial regions with different curvatures to measure the lengths with ultrasound and 3D-surface scans.

Results: In the frontal region, the supratrochlear and supraorbital artery coursed at an average of 15.5 ± 3.5 mm and 27.8 ± 5.3 mm lateral to the midline, respectively. In relation to the ipsilateral vertical glabellar line, the supratrochlear and supraorbital artery coursed laterally at an average distance of 9.5 ± 3.4 mm and 21.7 ± 4.8 mm, respectively. The mean diameter was 0.90 ± 0.02 mm for the supratrochlear artery and was 0.70 ± 0.02 mm for the supraorbital artery. The average distance to the skin surface (= depth of the artery) was 3.34 ± 0.6 mm for the supratrochlear artery and 3.54 ± 0.8 mm for the supraorbital artery. When the study participants were told to contract their corrugator supercilii muscles in the glabellar region ("frowning"), the supratrochlear artery moved more medially towards the midline and the ipsilateral vertical glabellar fold by an average of 3.1 mm and 1.8 mm, respectively. The supraorbital artery moved medially by an average of 3.7 mm to the midline and by 2.3 mm to the ipsilateral vertical glabellar line upon frowning.

In the perioral region, the superior and inferior labial arteries ran within the vermilion in 83.7% of all investigated cases (206 of 240 measurements). All examined arteries ran within the red lip in the midline measurement points (P2 in the upper lip and P5 in the lower lip). The average distance between the labial arteries and the vermilion border of the respective lip was 1.8 ± 2.5 mm. The mean diameter of the superior labial artery was 0.91 ± 0.2 mm in the lateral measurement points of the upper lip (P1 and P3) and 0.75 ± 0.1 mm in the medial measuring point (P2) of the arteries. The inferior labial artery showed an average diameter of 0.83 ± 0.2 mm in the lateral measurement points of the lower lip (P4 and P6) and 0.76 ± 0.2 mm in the medial measurement point (P5). These values indicated a narrowing of the arteries when coursing more medially. The most common course of both labial arteries was submucosally in 58.5% of the investigated cases. The second most common type was the intramuscular course (36.2%) followed by the subcutaneous course (5.3%). The average distance to the surface of the skin (= depth of the arteries) was 5.6 ± 1.3 mm for the superior labial artery and 5.2 ± 1.4 mm for the inferior labial artery.

The average measured length of the 20 mm - Steri-Strips^{TM} was 18.83 ± 0.08 mm for the ultrasound measurement and 19.89 ± 0.02 mm for the photographic 3D-scan measurement, regardless of the facial region, with $p < 0.0001$. Thus, the average difference to the standardized length of the reference point (20 mm) was 1.17 ± 0.3 mm for the ultrasound measurement and 0.11 ± 0.1 mm for the photographic 3D-scan measurement and the difference between both methods was 1.07 mm, regardless of analyzed facial region. In the frontal region (as an example of a “flat” facial region with less convexities and concavities) the difference was measured to be 0.59 mm (0.65 ± 0.4 mm for ultrasound and 0.06 ± 0.2 mm for 3D-scan) with $p < 0.0001$ between both measurements.

Conclusion: The previously postulated hypothesis that the supratrochlear artery typically courses in or directly next to the vertical glabellar line and that injections lateral to the vertical glabellar line can thus be considered safe, must be rejected based on the data obtained in this study. Both, the supratrochlear and supraorbital artery showed high degrees of variability in their topographical course. Especially, the great differences in the horizontal distance to the midline and vertical glabellar line make it almost impossible to anticipate the course of investigated arteries.

Furthermore, it was shown that the labial arteries do not course in a reliable inter-individual distance to the vermilion border. On basis of the obtained data, injections in the perioral region should preferably be carried out outside of the vermilion rather than inside of the vermilion as commonly performed in lip volumization procedures since both labial arteries are less likely to run there. Patient safety and treatment efficacy with soft-tissue filler injections in the frontal and perioral region as well as the preoperative planning of vascular-pedicled and free vascularized flaps in the facial area can be improved with help of knowledge gained in this study about average topographical vascular courses.

Additionally, a standardized algorithm for the analysis of individual vascular topography was presented here. Both methods used for distance measurements (ultrasound and photographic 3D-scans) were objectively compared with each other. It was shown that distance measurements obtained by ultrasound imaging can be used effectively for pre-operative planning in flat facial regions (e.g., frontal region). The highest extent of clinical applicability can be achieved by the combination with 3D surface scans as both methods allow to visualize “structures under the skin” (ultrasound imaging) and “above the skin” (3D-surface scans) to relate the vascular course with orientation marks on the skin of the patient.

5. Veröffentlichung I

Cosmetic Medicine

Aesthetic Surgery Journal
2020, Vol 40(12) 1327–1335

DOI: 10.1093/asj/sjaa137
www.aestheticsurgeryjournal.com
OXFORD
UNIVERSITY PRESS

Anatomy of the Superior and Inferior Labial Arteries Revised: An Ultrasound Investigation and Implication for Lip Volumization

Sebastian Cotofana, MD, PhD; Michael Alfertshofer;
Thilo L. Schenck, MD, PhD; Vince Bertucci, MD; Katie Beleznay, MD;
Benjamin Ascher, MD; Nirusha Lachmann, MD, PhD;
Jeremy B. Green, MD; Arthur Swift, MD; and Konstantin Frank, MD

Abstract

Background: Lips are considered a key element of facial attractiveness due to their central position in the face and their elemental role in verbal and nonverbal communication.

Objectives: The authors sought to provide clinically relevant information on the 3-dimensional pathway of the superior and inferior labial arteries within the lips to increase safety during labial soft tissue filler injections.

Methods: The study enrolled 41 healthy volunteers with a mean age of 26.17 ± 9.6 years and a mean body mass index of 23.09 ± 2.3 kg/m^2. Ultrasound imaging was performed at 6 different locations. The position of the labial arteries within the lips, depth of the arteries, cranio-caudal location of each artery in relation to the vermilion border, and diameter of the superior/inferior labial arteries were recorded.

Results: The most frequent location of both the superior and inferior labial arteries was the submucosal plane (58.5%) followed by intramuscular (36.2%) and subcutaneous (5.3%) planes. The depth of the superior labial artery in the upper lip was 5.6 ± 0.13 mm, whereas the depth of the inferior labial artery in the lower lip was 5.2 ± 0.14 mm. Both arteries were more frequently located within the red lip: upper lip (83% vs 18.7%) and lower lip (86.2% vs 13.8%). In the midline, the artery coursed within the red lip in all investigated volunteers.

Conclusions: Clinically, results of this study favor a superficial injection plane for lip volumization procedures. A perpendicular approach to the lip (coming from the cutaneous lip) might increase safety because the artery is located most frequently within the red lip.

摘要

背景

由于嘴唇在面部的中心位置以及在语言和非语言交流中的基本作用，嘴唇被认为是面部吸引力的关键因素。

目的

提供唇内上唇和下唇动脉三维路径的临床相关信息，以提高唇部软组织填充剂注射的安全性。

Dr Cotofana is an Associate Professor and Physician and Dr Lachmann is an Associate Professor, Department of Clinical Anatomy, Mayo Clinic College of Medicine and Science, Mayo Clinic, Rochester, MN. Mr Alfertshofer is a Medical Student and Drs Schenck and Frank are Physicians, Department for Hand, Plastic and Aesthetic Surgery, Ludwig – Maximilian University Munich, Germany. Dr Bertucci is a Physician, Division of Dermatology, University of Toronto, Toronto, Ontario, Canada. Dr Belezany is a Physician, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, British Columbia, Canada. Dr Ascher is a physician in private practice in Paris, France. Dr Green is a physician in private practice in Coral Gables, FL. Dr Swift is a physician in private practice in Montreal, Quebec, Canada.

Corresponding Author:
Dr Sebastian Cotofana, Department of Clinical Anatomy, Mayo Clinic College of Medicine and Science, Mayo Clinic, Stabile Building 9–38, 200 First Street, Rochester, MN, 55905, USA.
Email: cotofana.sebastian@mayo.edu;
Instagram: @professorsebastiancotofana

方法
本研究招募了 41 名健康志愿者，平均年龄 26.17 ± 9.6 岁，平均 BMI 为 23.09 ± 2.3 kg/m2。在 6 个不同的位置进行了超声成像。记录了唇动脉在唇内的位置、动脉的深度、每条动脉相对于唇红缘的头尾位置以及上/下唇动脉的直径。
结果
上唇动脉和下唇动脉最常见的部位是粘膜下平面（58.5%），其次是肌内平面（36.2%）和皮下（5.3%）平面。上唇-动脉在上唇的深度为 5.6±0.13mm，下唇动脉在下唇的深度为 5.2±0.14mm。两条动脉更常位于红唇内：上唇（83% 对 18.7%）和下唇（86.2% 对 13.8%）。在中线，所有接受调查的志愿者的动脉都位于红唇内。
结论
临床上，这项研究的结果支持一种浅表注射平面丰唇手术。由于动脉最常位于红唇内，因此垂直于唇部（来自唇部皮肤）可能会增加安全性。

Editorial Decision date: May 18, 2020; online publish-ahead-of-print May 29, 2020.

According to the annual statistic report released by The Aesthetic Society, a total of 810,240 soft tissue filler injections (unspecified) were performed in 2018 in the United States.[1] This high number is constantly increasing and is indicative of the high social demand for improved body image and desire for a young and attractive facial appearance. Although many areas of the face receive attention for aesthetic improvement,[2-6] the lips are considered a key element of facial attractiveness due to their central position in the face and their elemental role in verbal and nonverbal communication.[7-10]

Various techniques for improving lip contour and lip volume are currently performed employing needles or cannulas[11-13] utilizing superficial or deep injection[13,14] for an optimal aesthetic outcome. However, a recent anatomic study[14] revealed that in 58.3% of all injections performed, independent of the utilized injector (needle/cannula) and independent of the injected plane (submucosal, intramuscular, subcutaneous), the material was located in proximity to the superior/inferior labial arteries. This indicates a potential danger for adverse vascular events, including previously documented irreversible blindness.[15,16]

Previous studies have confirmed a variable course of the labial arteries within the lips describing the submucosal plane between the orbicularis oris muscle and oral mucosa as the most frequent plane of location for both the superior and inferior labial arteries (range, 42-86%)[10,17] followed by the intramuscular (range, 7-45%) and the subcutaneous plane (range, 0-5%).[10,17] These anatomical locations suggest that the subcutaneous plane (superficial plane of the lips) is a safer zone for injecting lip fillers because the artery is more commonly located deep to this plane.

Other clinically important information about the course of the labial arteries is the spatial relationship between them and the vermilion border. The vermilion border represents the boundary between the red lip and the cutaneous (hairy) lip and is frequently utilized for contouring and reshaping procedures. To date, there is no information available in the Caucasian population[17] obtained from noncadaveric investigations[2,18] on the cranio-caudal course of the labial arteries in relation to the vermilion border. Having this information available could guide practitioners to safer lip contouring and lip volumizing procedures because the probability of the 3-dimensional (3-D) pathway of the labial arteries could be estimated.

The objective of this ultrasound and 3-D surface scan imaging study performed in lip injection–naive volunteers was to provide clinically relevant information on the 3-D course of the superior and inferior labial arteries to increase safety during soft tissue filler injections of the lips.

METHODS

Study Sample

Volunteers were screened and not included in this analysis if previous minimally invasive injections of soft-tissue fillers or perioral neuromodulator treatments had been performed. Other exclusion criteria included facial surgeries, facial trauma, or any type of disease affecting the integrity of the facial anatomy. Volunteers were briefed on the aims, scope, and procedures of the study (ultrasound imaging), and each participant provided written informed consent for the utilization of both their data and associated images prior to their initiation into the study. The study was approved by the Institutional Review Board of Ludwig-Maximilian University Munich (IRB protocol number: 19–999). This study was conducted in accordance with regional laws of Germany maintaining good clinical practice. Ultrasound-based measurements were conducted between October 2019 and January 2020.

Ultrasound Imaging

Ultrasound imaging was performed with the volunteers in an upright (90°C) seated position employing an 18-MHz linear transducer (LOGIQ S7 Expert, GE Healthcare GmbH, Solingen, Germany). Measurements were performed without application of pressure to the skin as the transducer was placed into the visualization gel only without direct skin contact (Aquasonic Clear Ultrasound Gel, Parker Laboratories Inc., Fairfield, NJ). Six different locations were scanned (Figure 1): 3 in the upper lip and 3 in the lower lip according to a previously published protocol[10] (1 cm medial to each corner of the mouth and in the midline). The measured ultrasound positions were termed according to the clockwise sequence of the conducted measurements: P1 (paramedian right upper lip), P2 (midline upper lip), P3 (paramedian left upper lip), P4 (paramedian left lower lip), P5 (midline lower lip), and P6 (paramedian right lower lip).

The vermilion border (ie, the boundary between the red lip and the cutaneous [hairy] lip) was marked with a sticky gauze pad (R1547 Steri-Strip, 3M Deutschland GmbH, Neuss, Germany), which created a sonic shadow in the ultrasound images. This facilitated the identification of the cranio-caudal location of the vermilion border within the lip during ultrasound image analysis. To identify the labial arterial vasculature, the Doppler-mode of the ultrasound machine was utilized to differentiate arterial from venous structures (pulsatile arterial blood flow vs continuous venous blood flow) and to conduct measurements. The following parameters were evaluated:

- Position of the superior/inferior labial artery within the lip: submucosal, intramuscular, subcutaneous (Figures 2-5)
- Depth of the artery when measured from skin surface (in millimeters)
- Cranio-caudal location of the artery in relation to the vermilion border: within the red lip or outside the red lip (ie, within the cutaneous [hairy] lip) (in millimeters)
- Diameter of the superior/inferior labial artery (in millimeters)

The reliability (ie, concordance of repeated measurements in a particular set of samples)[19] of the ultrasound measurements was calculated by the intraclass correlation coefficient (ICC) in a subsample of n = 20 of the investigated population. Repeated measures of the depth of the artery at P1 and P3 revealed an ICC of 0.938.

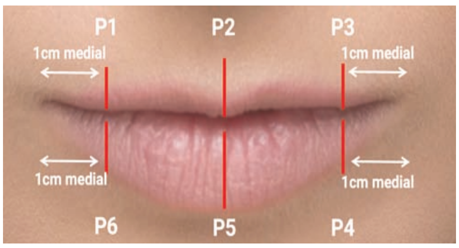

Figure 1. Measured locations for the upper lip (paramedian right upper lip [P1], midline upper lip [P2], and paramedian left upper lip [P3]) and the lower lip (paramedian left lower lip [P4], midline lower lip [P5], and paramedian right lower lip [P6]) exemplified in this 24-year-old female.

Statistical Analysis

Differences between measurements (upper vs lower lip; male vs female) were calculated utilizing independent Student's *t* test, whereas differences between the 6 different labial locations were calculated employing analysis of variance testing. Multifactorial influence (age, gender, body mass index [BMI]) on the depth of the arteries was investigated utilizing generalized linear models with robust estimator. Analyses were performed utilizing SPSS Statistics 26 (IBM, Armonk, NY), and statistical significance was defined as $P < 0.05$ to guide conclusions.

The term "submucosal" refers the the location of the artery between the orbicularis oris muscle and the oral mucosa. This location is closest to the teeth. The term "intramuscular" refers to the location of the artery within the 2 layers of the orbicularis oris muscle complex. The term "subcutaneous" refers to the location of the artery superficial to the orbicularis oris muscle; this includes the superficial location within the cutaneous (hairy) lip and the superficial location within the dry red lip portion. This location is furthest from the teeth.

RESULTS

Demographic Data

The study enrolled 41 healthy volunteers (20 males, 21 females; 40 Caucasians, 1 African-American) aged a mean 26.17 ± 9.6 years (range, 20-56 years) with a mean BMI of 23.09 ± 2.3 kg/m^2 (range, 17.8-28.4 kg/m^2).

Labial Arteries: Distribution in Position

In all 41 investigated study participants, the superior and the inferior labial arteries were consistently identified in both the upper and lower lips. The overall distribution of the position of the superior and the inferior labial artery within the lips when measured independent of gender, age, BMI, or labial position was 58.5% in the submucosal position, 36.2% in the intramuscular position, and 5.3% in the subcutaneous position.

The overall labial artery position with submucosal, intramuscular, and subcutaneous planes was 60.8%, 34.2%, and 5.0% in males and 56.3%, 38.1%, and 5.6% in females, respectively, with no differences between genders ($P = 0.775$). No statistically significant difference in this distribution was detected when comparing younger (≤26.17 years [mean age]) with older (>26.17 years) study participants ($P = 0.886$). The distribution of the position of

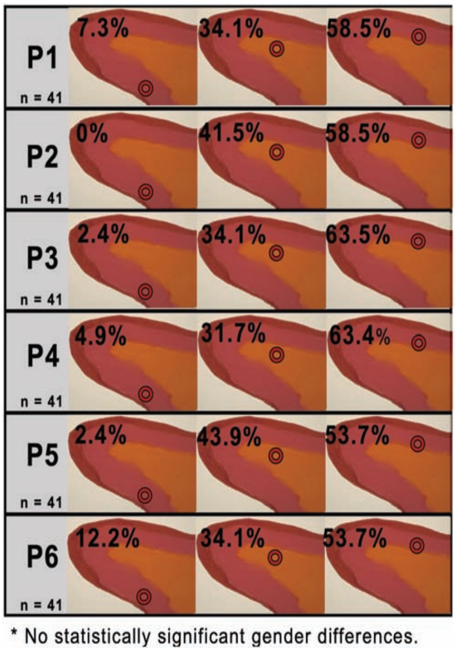

Figure 2. Schematic drawing (exemplified for the lower lip) of the 3 identified superior (paramedian right upper lip [P1], midline upper lip [P2], and paramedian left upper lip [P3]) and inferior (paramedian left lower lip [P4], midline lower lip [P5], and paramedian right lower lip [P6]) labial artery positions (subcutaneous/left, intramuscular/central, submucosal/right). Percentages represent the frequency of each of the identified locations in each of the 6 measured locations.

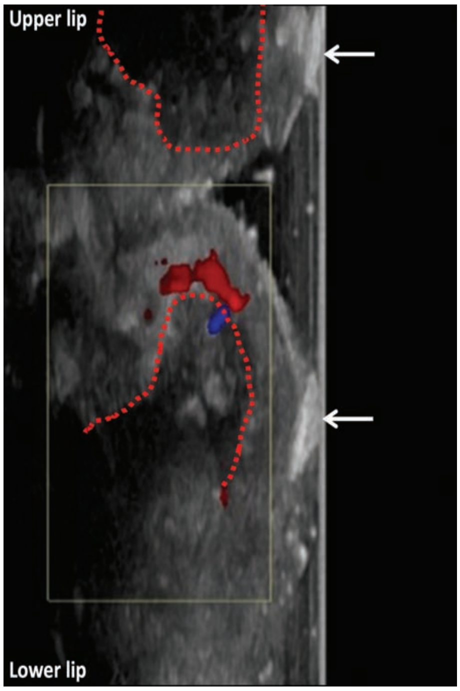

Figure 3. Doppler-supported ultrasound image showing the inferior labial artery in the subcutaneous position in this 29-year-old male study participant. White arrows indicate the position of the marked vermilion border. The orbicularis oculi muscle is highlighted by the red dotted line. The position of the measurement is shown on the lower right.

the superior labial artery in each of the measured positions (P1-P6) (submucosal, intramuscular, subcutaneous) is shown in Figure 2.

Labial Arteries: Depth

The depth of the labial arteries independent of age, gender, BMI, or labial position was 5.4 ± 1.4 mm. In males, the depth was 5.7 ± 1.4 mm, whereas in females it was 5.1 ± 1.3 mm ($P < 0.001$). The depth of the superior labial artery in the upper lip was 5.6 ± 1.3 mm (5.9 ± 1.5 mm vs 5.3 ± 1.1 mm in females; $P = 0.011$), whereas the depth of the inferior labial artery in the lower lip was 5.2 ± 1.4 mm (5.6 ± 1.4 mm in males vs 4.9 ± 1.5 mm in females; $P = 0.013$). The overall difference in depth between the upper and the lower lip was statistically significant ($P = 0.042$), indicating that the artery within the lower lip is located more superficially than in the upper lip. Interestingly, the depth varied significantly between each of the 6 investigated labial positions ($P < 0.001$). Detailed information of the depth of the labial arteries in each specific location is presented in Table 1.

Utilizing generalized linear models, we identified that the depth of the artery (independent of whether superior or inferior labial) significantly increased with increasing BMI (odds ratio = 1.01, 95% confidence interval = 1.001 – 1.019, $P = 0.036$) and male gender (odds ratio = 1.05, 95% confidence interval = 1.006 – 1.090, $P = 0.023$).

Labial Arteries: Cranio-Caudal Location

The mean overall distance independent of age, gender, and BMI of the artery to the vermilion border was 1.8 ± 2.5 mm. In n = 206 measurements (6 locations measured in 41 volunteers = 246 total) (83.7%), the artery was located within the red lip at a mean distance of 2.6 ± 1.5 mm when measured from the vermilion border. In n = 40 measurements (15.3%), the artery was located outside the red

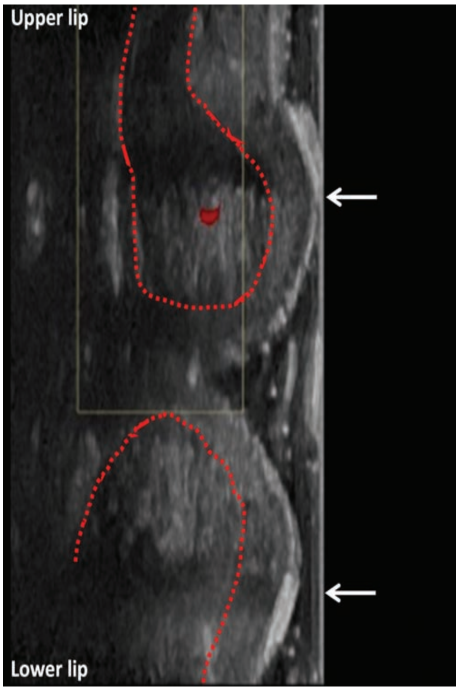

Figure 4. Doppler-supported ultrasound image showing the inferior labial artery in the intramuscular position in this 29-year-old female study participant. White arrows indicate the position of the marked vermilion border. The orbicularis oculi muscle is highlighted by the red dotted line. The position of the measurement is shown on the lower right.

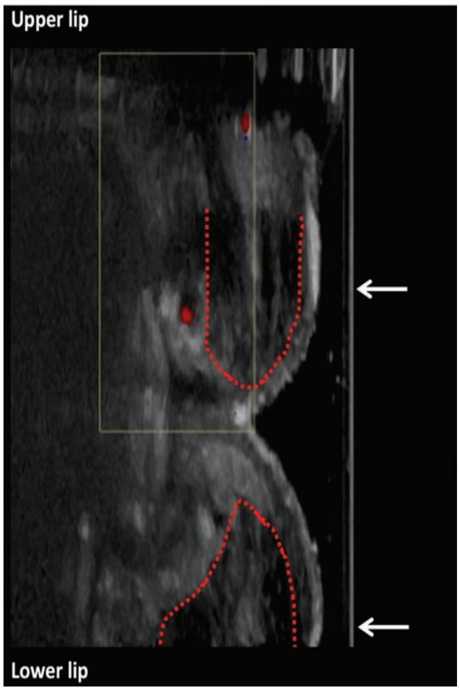

Figure 5. Doppler-supported ultrasound image showing the inferior labial artery in the submucosal position in this 24-year-old female study participant. White arrows indicate the position of the marked vermilion border. The orbicularis oculi muscle is highlighted by the red dotted line. The position of the measurement is shown on the lower right.

lip (= within the cutaneous [hairy] lip) with a mean distance of 2.4 ± 2.0 mm measured from the vermilion border (Figures 6-8).

In the upper lip, the superior labial artery was identified in n = 100 measurements (81.3%) within the red lip with a mean distance of 2.2 ± 1.5 mm and in n = 23 measurements (18.7%) outside (= cranial) the red lip, having a mean distance of 2.8 ± 2.0 mm measured from the vermilion border. No statistically significant difference between genders was observed ($P = 0.718$). Interestingly, in the midline of the upper lip, the artery was detected within the red lip in 100% of cases.

In the lower lip, the inferior labial artery was identified in n = 106 measurements (86.2%) within the red lip with a mean distance of 3.0 ± 1.4 mm to the vermilion border and in n = 17 cases (13.8%) outside the red lip and within the cutaneous (hairy) lip having a mean distance of 2.0 ± 2.0 mm measured from the vermilion border. This distribution did not display a statistically significant difference between genders ($P = 0.712$). In the midline of the lower lip, the artery was detected within the red lip in 100% of cases (Figures 6-8 and Table 2).

Labial Artery: Diameter

The mean overall diameter of the labial arteries was 0.83 ± 0.19 mm. The superior labial artery had a mean diameter of 0.86 ± 0.20 mm, whereas the inferior labial artery had a mean diameter of 0.81 ± 0.16 mm ($P = 0.021$). The mean diameter of the superior labial artery in males was 0.87 ± 0.17 mm, whereas that in females was 0.85 ± 0.22 mm ($P = 0.524$). The mean diameter of the inferior labial artery was 0.83 ± 0.16 mm in males, whereas in females it was 0.79 ± 0.16 mm ($P = 0.157$) (Figure 9).

The superior labial artery has a significantly smaller diameter in the midline of the upper lip (P2) (0.75 ± 0.14 mm) compared with both the paramedian (P1, P3) locations (0.92 ± 0.17 mm and 0.91 ± 0.22 mm, respectively; $P < 0.002$). The inferior labial artery likewise had a smaller diameter in the midline of the lower lip (P5) (0.76 ± 0.16 mm compared with both the paramedian locations (P4, P6)

Table 1. Depth of the Superior (P1-P3) and Inferior (P4-P6) Labial Artery at the Respective Locations for Males and Females

	P1	P2	P3	P4*	P5	P6
Males	0.58 ± 0.15	0.61 ± 0.17	0.59 ± 0.12	0.60 ± 0.14	0.54 ± 0.11	0.54 ± 9.15
Females	0.54 ± 0.11	0.55 ± 0.11	0.51 ± 0.13	0.51 ± 0.15	0.50 ± 0.14	0.48 ± 0.15

Statistically significant differences are indicated via an asterisk. P1, paramedian right upper lip; P2, midline upper lip; P3, paramedian left upper lip; P4, paramedian left lower lip; P5, midline lower lip; P6, paramedian right lower lip.

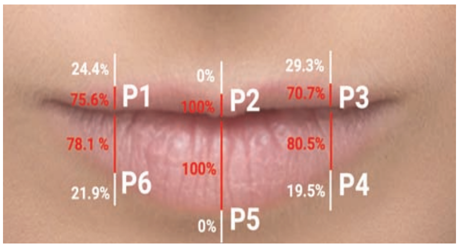

Figure 6. Distribution of the frequency of the arterial location within the red lip (red numbers) vs the cutaneous (hairy) lip (white numbers) within each of the 6 measured labial locations exemplified in this 24-year-old female. P1, paramedian right upper lip; P2, midline upper lip; P3, paramedian left upper lip; P4, paramedian left lower lip; P5, midline lower lip; P6, paramedian right lower lip.

(0.84 ± 0.14 mm and 0.82 ± 0.18 mm, respectively) but failed to reach statistical significance ($P > 0.05$).

DISCUSSION

This ultrasound and 3-D surface scan imaging-based investigation was conducted in 41 aesthetic procedure–naïve volunteers. The results revealed that the most frequent location of both the superior and inferior labial arteries was within the submucosal plane (ie, between the orbicularis oris muscle and oral mucosa; seen in 58.5%) followed by the intramuscular (36.2%) and the subcutaneous position (5.3%) without statistically significant difference between genders. In the lower lip, the artery tended to be slightly more superficial compared with the upper lip (submucosal, intramuscular, subcutaneous): 56.9%, 35.8%, and 7.3% vs 60.2%, 36.6%, and 3.3%, respectively, which was confirmed by the performed depth measurements. The depth of the superior labial artery in the upper lip was 5.6 ± 1.3 mm, whereas the depth of the inferior labial artery was 5.2 ± 1.4 mm. However, it was identified that the depth of the artery (independent whether superior or inferior labial) significantly increased with increasing BMI ($P = 0.036$) and male gender ($P = 0.023$). Evaluating the course of the arteries in relation to the vermilion border, it was found that in the upper lip the superior labial artery was more frequently located within the red lip (83% vs 18.7%) with a mean distance (measured in the frontal plane) of 2.2 ± 1.5 mm from the vermilion border (no gender differences). In the lower lip, the inferior labial artery was likewise more frequently located within the red lip (86.2% vs 13.8%) with a mean distance (measured in the frontal plane) of 2.0 ± 2.0 mm from the vermilion border (no gender differences). Of note, in the midline of both the upper and the lower lip, the artery was detected in all of the measured cases (100%) to course within the red lip. The superior labial artery had a significantly larger mean diameter compared with the inferior labial artery (0.86 ± 0.20 mm vs 0.81 ± 0.16 mm; $P = 0.021$). However, in the midline of both the upper and the lower lip (P2 and P4), the diameter of the artery was significantly smaller than the laterally located paramedian locations.

Strengths of this investigation are the gender-balanced study population with n = 20 males and n = 21 females and that the investigated patients were young (mean value: 26.17 years). This allows conclusions about normal lip anatomy that are not affected by age-related changes. Another strength is the utilization of standardized measuring location, which was previously shown to provide reliable measurements when evaluating the course of the superior/inferior labial arteries within the lips. Another strength of the study is the noninvasive nature of the ultrasound imaging. Real-time measurements were obtained without skin contact and applied pressure (ie, sound waves were transmitted via the visualization gel, preserving the original tissue thickness).

Limitations of the study are the small sample size and the methodology applied. Ultrasound-based measurements are subject to observer bias and might have a low reproducibility if performed by another investigator. To assure consistency throughout all measurements performed in this study, 1 investigator conducted the scans and performed all measurements (ICC = 0.938) to reduce this bias. Another potential limitation of the study is the young age of the investigated population and the limited ethnic diversity (n = 40 Caucasians and n = 1 African-American). The relative young age of the study sample might not reflect the regular clientele seeking aesthetic treatments. This study is designed to describe the normal anatomy of the labial arteries, and a sample not affected by age would thus provide the most reliable data. It is not expected that the

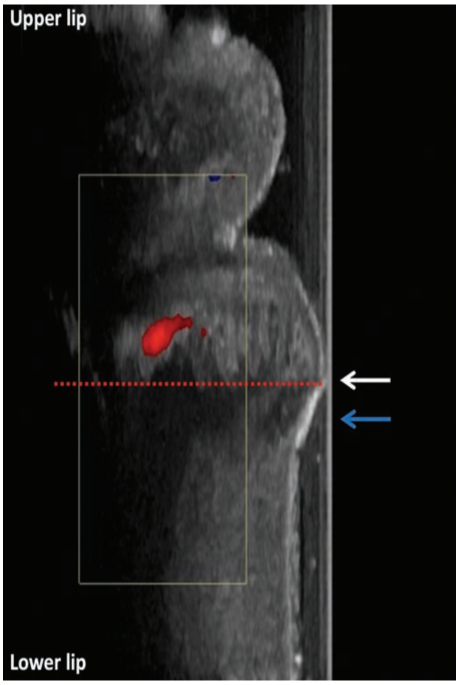

Figure 7. Doppler-supported ultrasound image showing the inferior labial artery (red signal) in the intramuscular position cranial to the vermilion border (white arrow/red dotted line) in this 24-year-old male study participant. The position of the measurement is shown on the lower right. The blue arrow points to the gauze that was utilized to mark the vermilion border.

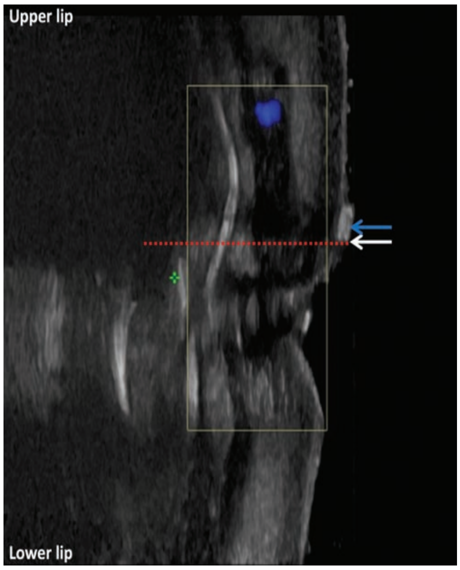

Figure 8. Doppler-supported ultrasound image showing the superior labial artery (blue signal) in the intramuscular position cranial to the vermilion border (white arrow/red dotted line) in this 25-year-old male study participant. The position of the measurement is shown on the lower right. The blue arrow points to the gauze that was utilized to mark the vermilion border.

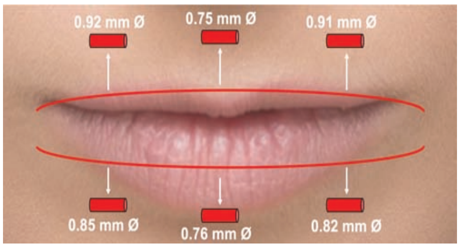

Figure 9. Shown is the diameter of the labial artery at its respective locations in the upper and the lower lip exemplified in this 24-year-old female.

position of the labial arteries in relation to the orbicularis oris muscles changes over time. Future studies, however, will need to generate information about whether the age-related elongation of the lips influence the position of the artery in relation to the vermilion border and whether this varies between different ethnic groups.

The results of this study confirm the findings seen in previous cadaveric[10,18] and another ultrasound-based investigation conducted in an Asian population.[17] Both the superior and the inferior labial arteries were most frequently identified to run deep within the lips located between the orbicularis oris muscle and the oral mucosa in the submucosal plane. This relationship was consistent across genders and age. Because similar results were observed from the present study investigating a relatively young cohort (n = 41, 26.17 ± 2.3 years) and a previous cadaveric study (conducted in n = 193 cadavers[10]) applying the same measurements, it could be assumed that age would not affect the position (ie, submucosal, intramuscular, subcutaneous plane) of the artery. From an anatomic perspective, this consistency would be plausible. The relation of the superior labial artery to the vermillion border, however, might be affected by age. It is widely accepted that the upper lip elongates with increasing age.[20,21] It could be speculated that due to the unrolling of the orbicularis oris muscle, the

Table 2. Frequency of the Location of the Superior (P1-P3) and Inferior (P4-P6) Labial Artery at the Respective Locations for Males and Females in Relation to the Vermilion (Above/Within)

	P1		P2		P3		P4		P5		P6	
	Above	Within	Above	Within	Above	Within	Above	Within	Above	Within	Above	Within
Male	4	16	0	20	8	12	3	17	0	20	6	14
Females	7	14	0	21	4	17	6	15	0	21	2	19

Statistically significant differences are indicated via an asterisk. P1, paramedian right upper lip; P2, midline upper lip; P3, paramedian left upper lip; P4, paramedian left lower lip; P5, midline lower lip; P6, paramedian right lower lip.

artery might descend within the labial soft tissues and change its position from the hairy (cutaneous) lip into the red lip (ie, from cranial to caudal of the vermilion border). Future studies will need to investigate this process for the upper and the lower lip separately. However, a cross-sectional study design might be biased by inter-individual variation of the labial arteries and might confound results. Longitudinal studies might be better suited, but they are difficult to enroll with a meaningful interval between the baseline and the follow-up assessment.

However, the present study could not confirm previous findings that reported a more superficial course of both the superior and inferior labial arteries in the midline.[10] It was identified that the distribution (ie, submucosal, intramuscular, subcutaneous plane) did not significantly alter between the 6 measured positions, indicating that a similar distribution of the artery in relation to the orbicularis oris muscle across both lips can be expected; this is in line with recent reports.[17,18] A reason for this discrepancy could be the smaller sample size (n = 193 vs n = 41) of this study and the inclusion of healthy (living) volunteers. However, the results presented herein are consistent with recent reports, which likewise did not observe a more superficial plane of the arteries in the midline.

The present study confirms results obtained from an Asian population[17] that reported that the artery courses slightly more superficially in the lower lip than in the upper lip. The measured distance from the surface was 5.6 ± 1.3 mm for the upper lip, whereas the depth of the inferior labial artery in the lower lip was 5.2 ± 1.4. Despite reaching statistical significance ($P = 0.042$), the results must be interpreted with care because a 0.04-mm difference might yield less clinical impact. However, it must be noted that multivariate generalized linear models revealed that the depth of the arteries is significantly influenced by an individual's BMI, with higher BMIs increasing the distance between the skin surface and artery. Future studies intending to investigate the depth of the artery should adjust their results to the BMI of the investigated patient and guard against reporting unadjusted values on arterial depth.

Clinically, the results suggest that a safer plane for injecting soft tissue fillers is the subcutaneous plane because the artery is located across both the upper and the lower lip deep in the submucosal plane. Despite concerns of not achieving the best volumizing results, especially in volume-deficient lips, the subdermal plane should be targeted. From an anatomic perspective, injecting deep into the body of the lip carries a higher risk to inject intra-arterially because the needle/cannula is inserted blindly. Injecting superficially can be visually controlled because the tip of the needle/cannula is still visible. This technique can be employed to control superficial as opposed to deep product placement. Positioning the product superficially and closer to the wet/dry mucosal transition line can evert the lip because the lip resides against the other lip or the teeth.

The present study provides data on the cranio-caudal relationship of the arteries to the vermilion border. We identified that the artery is more frequently located within the red lip as opposed to the cutaneous (hairy) lip (upper lip [83% vs 18.7%] and lower lip [86.2% vs 13.8%]). Especially in the midline, this relationship was clearer because the artery coursed within the red lip in all investigated volunteers (100%). These findings are novel because they reveal that the artery can be less frequently encountered cranial (for the upper lip) and inferior (for the lower lip) to the vermilion border. Clinically, dermal access to the lip could be more safely achieved by injecting perpendicular into the lip rather than following the vermilion border. This would favor a perpendicular approach to the artery (reduced contact area with the vessel wall) and an injection trajectory that is less likely to contact the arterial pathway.

The diameter of the artery was measured to be larger laterally than in the midline both for the upper lip (0.91 mm vs 0.75 mm) and the lower lip (0.83 mm vs 0.76 mm). This decreasing diameter is typical for the anastomotic nature of both arteries because left and right sides most frequently approximate toward the midline. These results are in line with a recent cadaveric study that similarly reported a narrowing in diameter of the superior labial artery toward the midline. Clinically, it could be assumed that the risk for injecting into an artery could be potentially smaller because the diameter in the midline is smaller than laterally. Nevertheless, care should be taken when injecting the lips and following current standards of safety with injecting small boluses, injecting with minimal plunger pressure, conducting pre-injection aspiration, and observing the surrounding tissue for discoloration during the injection process.

CONCLUSIONS

The results revealed that the most frequent location of both the superior and inferior labial arteries is the submucosal plane (58.5%) followed by the intramuscular (36.2%) and the subcutaneous position (5.3%). The depth of the superior labial artery in the upper lip was 5.6 ± 1.3 mm, whereas the depth of the inferior labial artery in the lower lip was 5.2 ± 1.4 mm. The artery is more frequently located within the red lip than in the cutaneous (hairy) lip (upper lip [83% vs 18.7%] and lower lip [86.2% vs 13.8%]); this relationship was more evident especially in the midline, because the artery coursed purely within the red lip in all investigated volunteers (100%). Clinically, these results support an injection technique that is more superficial in the subcutaneous plane independent of labial position. A perpendicular approach to the lip might be safer because the artery courses more frequently within the red lip.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. The American Society for Aesthetic Plastic Surgery's Cosmetic Surgery National Data Bank: Statistics 2018. *Aesthet Surg J*. 2019;39(Suppl_4):1-27.
2. Sykes JM, Cotofana S, Trevidic P, et al. Upper face: clinical anatomy and regional approaches with injectable fillers. *Plast Reconstr Surg*. 2015;136(5 Suppl):204S-218S.
3. Cotofana S, Schenck TL, Trevidic P, et al. Midface: clinical anatomy and regional approaches with injectable fillers. *Plast Reconstr Surg*. 2015;136(5 Suppl):219S-234S.
4. Braz A, Humphrey S, Weinkle S, et al. Lower face: clinical anatomy and regional approaches with injectable fillers. *Plast Reconstr Surg*. 2015;136(5 Suppl):235S-257S.
5. Matarasso SL, Carruthers JD, Jewell ML; Restylane Consensus Group. Consensus recommendations for soft-tissue augmentation with nonanimal stabilized hyaluronic acid (Restylane). *Plast Reconstr Surg*. 2006;117(3 Suppl):3S-34S; discussion 35S.
6. Sundaram H, Liew S, Signorini M, et al.; Global Aesthetics Consensus Group. Global aesthetics consensus: hyaluronic acid fillers and botulinum toxin type A-recommendations for combined treatment and optimizing outcomes in diverse patient populations. *Plast Reconstr Surg*. 2016;137(5):1410-1423.
7. Burrows AM. The facial expression musculature in primates and its evolutionary significance. *Bioessays*. 2008;30(3):212-225.
8. Charles Finn J, Cox SE, Earl ML. Social implications of hyperfunctional facial lines. *Dermatol Surg*. 2003;29(5):450-455.
9. Mannino GN, Lipner SR. Current concepts in lip augmentation. *Cutis*. 2016;98(5):325-329.
10. Cotofana S, Pretterklieber B, Lucius R, et al. Distribution pattern of the superior and inferior labial arteries: impact for safe upper and lower lip augmentation procedures. *Plast Reconstr Surg*. 2017;139(5):1075-1082.
11. Sarnoff DS, Gotkin RH. Six steps to the "perfect" lip. *J Drugs Dermatol*. 2012;11(9):1081-1088.
12. San Miguel Moragas J, Reddy RR, Hernández Alfaro F, Mommaerts MY. Systematic review of "filling" procedures for lip augmentation regarding types of material, outcomes and complications. *J Craniomaxillofac Surg*. 2015;43(6):883-906.
13. Surek CC, Guisantes E, Schnarr K, Jelks G, Beut J. "No-touch" technique for lip enhancement. *Plast Reconstr Surg*. 2016;138(4):603e-613e.
14. Ghannam S, Sattler S, Frank K, et al. Treating the lips and its anatomical correlate in respect to vascular compromise. *Facial Plast Surg*. 2019;35(2):193-203.
15. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, Jones D. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J*. 2019;39(6):662-674.
16. Beleznay K, Carruthers JDA, Humphrey S, Jones D. Avoiding and treating blindness from fillers. *Dermatologic Surg*. 2015;41(10):1097–1117.
17. Lee KL, Lee HJ, Youn KH, Kim HJ. Positional relationship of superior and inferior labial artery by ultrasonography image analysis for safe lip augmentation procedures. *Clin Anat*. 2020;33(2):158-164.
18. Money SM, Wall WB, Davis LS, Edmondson AC. Lumen diameter and associated anatomy of the superior labial artery with a clinical application to dermal filler injection. *Dermatol Surg*. 2020;46(5):678-684.
19. Popović ZB, Thomas JD. Assessing observer variability: a user's guide. *Cardiovasc Diagn Ther*. 2017;7(3):317-324.
20. Iblher N, Kloepper J, Penna V, Bartholomae JP, Stark GB. Changes in the aging upper lip - a photomorphometric and MRI-based study (on a quest to find the right rejuvenation approach). *J Plast Reconstr Aesthetic Surg*. 2008;61(10):1170-1176.
21. Ramaut L, Tonnard P, Verpaele A, Verstraete K, Blondeel P. Aging of the upper lip: Part I: a retrospective analysis of metric changes in soft tissue on magnetic resonance imaging. *Plast Reconstr Surg*. 2019;143(2):440-446.

6. Veröffentlichung II

Cosmetic Medicine

Relationship Between Vertical Glabellar Lines and the Supratrochlear and Supraorbital Arteries

Aesthetic Surgery Journal
2020, Vol 40(12) 1341–1348

DOI: 10.1093/asj/sjaa138
www.aestheticsurgeryjournal.com
OXFORD
UNIVERSITY PRESS

Sebastian Cotofana, MD, PhD; Michael Alfertshofer; Konstantin Frank, MD; Vince Bertucci, MD; Katie Beleznay, MD; Andreas Nikolis, MD; Jonathan Sykes, MD; Arthur Swift, MD; Nirusha Lachman, PhD; and Thilo L. Schenck, MD, PhD

Abstract

Background: Glabellar soft tissue filler injections have been shown to be associated with a high risk of causing injection-related visual compromise.

Objectives: The aim of this study was to identify the course of the superficial branch of the supratrochlear and of the deep branch of the supraorbital artery in relation to the ipsilateral vertical glabellar line and to test whether an artery is located deep to this line.

Methods: Forty-one healthy volunteers with a mean age of 26.17 [9.6] years and a mean BMI of 23.09 [2.3] kg/m^2 were analyzed. Ultrasound imaging was applied to measure the diameters, distance from skin surface, distance between the midline, distance between vertical glabella lines, and the cutaneous projection of the supratrochlear/supraorbital arteries at rest and upon frowning.

Results: The mean distance between the superficial branch of the supratrochlear artery and the ipsilateral vertical glabellar line was 10.59 [4.0] mm in males and 8.21 [4.0] mm in females, whereas it was 22.38 [5.5] mm for the supraorbital artery in males and 20.73 [5.6] mm in females. Upon frowning, a medial shift in supratrochlear arterial position of 1.63 mm in males and 1.84 mm in females and of 3.9 mm in supraorbital arterial position for both genders was observed. The mean depth of the supratrochlear artery was 3.34 [0.6] mm at rest, whereas the depth of the supraorbital artery was 3.54 [0.8] mm.

Conclusions: The hypothesis that injecting soft tissue fillers next to the vertical glabellar line is safe because the supratrochlear artery courses deep to the crease should be rejected. Additionally, the glabella and the supraorbital region should be considered as an area of mobile, rather than static, soft tissues.

Editorial Decision date: May 18, 2020; online publish-ahead-of-print May 29, 2020.

Dr Cotofana is an Associate Professor and Physician and Dr Lachman is a Full Professor and Chair, Department of Clinical Anatomy, Mayo Clinic College of Medicine and Science, Rochester, MN, USA. Mr Alfertshofer is a medical student and Drs Frank and Schenck are Physicians, Department for Hand, Plastic, and Aesthetic Surgery, Ludwig- Maximilians University Munich, Munich, Germany. Dr Bertucci is a Physician, Division of Dermatology, University of Toronto, Toronto, Ontario, Canada. Dr Beleznay is a Physician, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada. Dr Nikolis is a Physician, Erevna Innovations Inc, Clinical Research Unit, Montreal, Quebec, Canada; and the Division of Plastic Surgery, McGill University, Montreal, Quebec, Canada. Dr Sykes is a Physician, Facial Plastic and Reconstructive Surgery, UC Davis Medical Centre, Sacramento, CA, USA. Dr Swift is a Physician in private practice in Montreal, Quebec, Canada.

Corresponding Author:
Dr Sebastian Cotofana, Associate Professor of Anatomy, Department of Clinical Anatomy, Mayo Clinic College of Medicine and Science, Mayo Clinic, Stabile Building 9-38, 200 First Street, Rochester, MN 55905, USA.
E-mail: cotofana.sebastian@mayo.edu;
Instagram: @professorsebastiancotofana

According to the annual statistics reported by The Aesthetic Society,[1] more than US$1 billion was spent in 2018 on aesthetic treatments with injectable agents such as neuromodulators or soft tissue fillers. This large number is indicative of the high demand for enhanced facial and body attractiveness.[2-4]

Concomitant with the high number of facial injections performed, published reports of adverse events have also increased, with tissue loss (necrosis) and injection-related visual compromise (irreversible blindness) representing the most devastating of all possible outcomes.[5-7] The currently accepted pathophysiologic mechanism behind those severe adverse events is that soft tissue fillers are injected into the arterial vascular system and are transported to watershed areas where the terminal circulation is affected. The arterial vascular obstruction can be related to the material itself, to intravascular damage of the vessels' intima, and/or to activation of the various blood coagulation pathways.[8,9] This has most severe effects in areas lacking additional supportive arterial circulation or in tissue with greatest need of a constant arterial blood supply such as the retina.

The retina receives arterial blood supply from various branches of the ophthalmic artery.[8] These retinal arteries are connected to branches of the external carotid system and to branches of the contralateral side. The area where those arteries form anastomotic connections is the glabella and the supraorbital region with major involvement of branches of the supratrochlear and supraorbital arteries.

The glabella was identified to be one of the facial regions presenting the greatest risk of injection-related visual compromise during injection of soft tissue fillers.[5,6] This could be attributed to its complex 3-dimensional arterial vascular network, which includes the central artery (of the forehead), the paracentral artery, the superficial branch of the supratrochlear artery, and branches of the supraorbital artery.[10-12]

Recent research has suggested utilizing the vertical glabellar line as a landmark for soft tissue filler injections to increase safety. It is hypothesized that the superficial branch of the supratrochlear artery is located deep to the crease and injections next to the crease are safer because the artery is not located there.[13]

The objective of the present investigation was to identify the course of the superficial branch of the supratrochlear and the deep branch of the supraorbital artery in relation to the ipsilateral vertical glabellar line and to determine whether either of the arteries is located deep to the glabellar line or courses elsewhere. The results will verify the hypothesis that injecting soft tissue filler away from the glabellar crease is a safe procedure given previous findings that the artery is located deep to the crease.

METHODS

Study Sample

Study participants were recruited from the pool of consecutive patients of the Department of Hand, Plastic, and Aesthetic Surgery at Ludwig-Maximilians University Munich. Participants were screened and excluded from participation in this study if soft tissue fillers had previously been injected into the glabella, the supraorbital area, or the forehead. Additionally, patients were excluded if neuromodulators had been injected into the glabella, the forehead, or the supraorbital area in the preceding 6 months. Other exclusion factors were facial surgeries, facial trauma, or any type of disease affecting the integrity of their facial anatomy. Volunteers were informed about the aims and methods of this investigation (ultrasound imaging). Each volunteer provided written informed consent for the use of both their data and associated images prior to their initiation into the study. The study was approved by the Institutional Review Board of Ludwig-Maximilians University Munich (IRB protocol number 19-999). This study was conducted in accordance with regional laws (Germany) and good clinical practice. Ultrasound-based measurements were conducted between October 2019 and January 2020.

Ultrasound Imaging

Volunteers were seated in an upright (90°) position during the ultrasound imaging of their glabellar and supraorbital region. An 18-MHz linear transducer (LOGIQ S7 Expert; GE Healthcare GmbH, Solingen, Germany) was used for all imaging procedures, which were performed by the same investigator (M.A.) to ensure consistency throughout the measurements. Visualization of the vascular structures (ie, supratrochlear and supraorbital arteries) and distance and depth measurements were performed without application of pressure to the skin as the transducer was only placed into the visualization gel without direct skin contact (Aquasonic Clear Ultrasound Gel; Parker Laboratories Inc, Fairfield, NJ) (Figure 1).

The midline and the location of the vertical glabellar lines were marked with a portion of a sticky gauze pad (R1547 Steri-Strip; 3M Deutschland GmbH, Neuss, Germany) to create a sonic shadow in the ultrasound images to facilitate distance measurements. The vertical glabellar lines were identified after maximum contraction of the glabella when the volunteers were asked to frown as hard as possible or to look angry. This skin location of the formed crease was marked and served as an indicator during measurements performed at rest.

The arteries of interest were the superficial branch of the supratrochlear artery[9,14] (hereinafter referred to as the

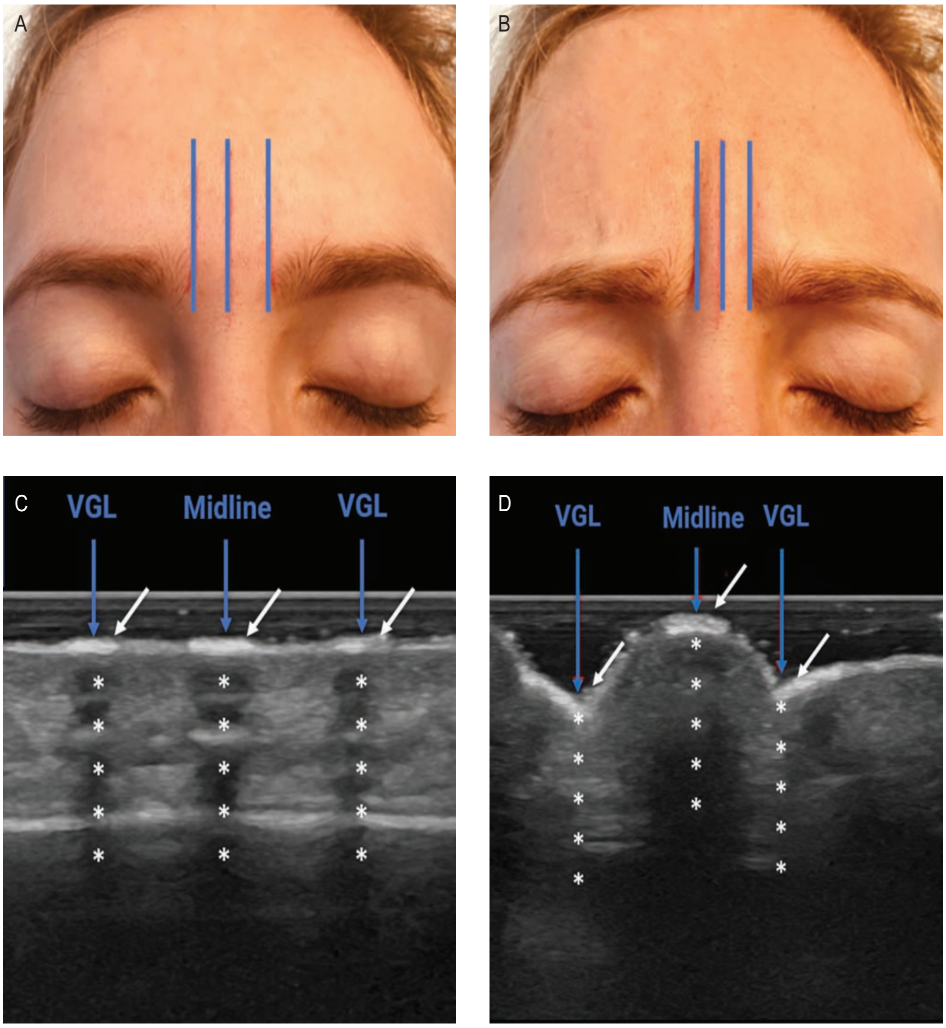

Figure 1. (A) Photograph showing the relaxed (not contracted) glabellar region of a 24-year-old female while resting. The previously identified and marked vertical glabellar lines (right and left) and the midline (center) are indicated by blue lines. (B) Photograph showing the glabellar region of the same 24-year-old female as in Figure 1A upon frowning. The vertical glabellar lines (right and left) and the midline (center) are indicated by blue lines. Note that the vertical glabellar lines moved closer to the center. (C) Ultrasound image of the glabellar region shown in (A). The vertical glabellar lines (VGL) and the midline have been marked with steri-strips (white arrows), which created an ultrasonic shadow (white asterisks). (D) Ultrasound image of the glabellar region shown in (B). The VGL and the midline have been marked with steri-strips (white arrows), which created an ultrasonic shadow (white asterisks).

supratrochlear artery) and the deep branch of the supraorbital artery (hereinafter referred to as the supraorbital artery).[9,14] Both arteries were first identified upon emergence from their respective foramina/notch (supratrochlear and supraorbital) and followed until they reached a horizontal line passing through the vertical middle of the eyebrow at rest. This ensured that during ultrasound measurements the medial supraorbital arterial pathways were not confused with the lateral supratrochlear pathways. The following measurements were recorded at the horizontal mid-eyebrow level with the distance measurement and color-coded Doppler-imaging functions of the ultrasound device:

- diameters (mm) of both left and right supratrochlear/supraorbital arteries;
- distance (mm) between skin surface and the supratrochlear/supraorbital arteries as visualized upon color-encoded Doppler imaging at rest and upon frowning;
- distance (mm) between the midline and the cutaneous projection of both left and right supratrochlear/supraorbital arteries at rest and upon frowning;
- distance (mm) between vertical glabellar lines and the cutaneous projection of both left and right supratrochlear/supraorbital arteries at rest and upon frowning.

Repeated measures were performed in a subsample (n = 20) of the total sample to calculate the reliability of the ultrasound-based measurement and revealed an intraclass correlation coefficient (ICC) of 0.938.

Statistical Analysis

Differences between measurements (left vs right side; male vs female) were calculated by *t* test, and between resting and frowning parameters by paired *t* test. Multivariate analyses were performed with generalized linear models with a robust estimator and adjustment for age, body mass index (BMI), and forehead width. Analyses were performed with SPSS Statistics version 26 (IBM, Armonk, NY) and differences were considered statistically significant at $P \leq 0.05$ to guide conclusions.

RESULTS

Demographic Data

The study enrolled 41 healthy volunteers (20 males, 21 females; 40 Caucasians, 1 Afro-American) with a mean [standard deviation] age of 26.17 [2.3] years (range, 20-56 years) and a mean BMI of 26.17 [2.3] kg/m^2 (range, 17.8-28.4 kg/m^2).

Diameter of Arteries

The mean diameter of the supratrochlear artery was 0.90 [0.02] mm (range, 0.5-1.3 mm) and the mean diameter of the supraorbital artery was 0.70 [0.2] mm (range, 0.5-1.4 mm) when measured at the horizontal mid-eyebrow level.

Depth of Arteries

The mean distance between skin surface and the supratrochlear artery at the horizontal mid-eyebrow level was 3.34 [0.6] mm (range, 1.8-4.6 mm) at rest and 3.77 [0.7] mm (range, 2.1-5.4 mm) upon frowning ($P < 0.001$); ie, the depth of the the supratrochlear artery increased by 0.43 mm on frowning. The mean distance between the skin surface and the supraorbital artery was 3.54 [0.8] mm (range, 2.2-6.0 mm) at rest and 3.93 [1.0] mm (range, 1.8-6.3 mm) upon frowning ($P < 0.001$); ie, the depth of the the supraorbital artery increased by 0.39 mm on frowning. No statistically significant difference was observed between genders and side. Calculating generalized linear models with adjustment for age, BMI, and forehead width revealed no statistical influence on the depth for the supratrochlear artery. However, BMI significantly increased the depth of supraorbital artery (odds ratio, 1.01; 95% CI, 1.00-1.02; $P = 0.003$).

Distance of Vertical Glabellar Line from the Midline

The mean distance of the vertical glabellar line from the midline at rest was 5.55 [1.8] mm (range, 2.5-12.4 mm) in males and 6.59 [1.8] mm (range, 3.7-12.5 mm) in females ($P = 0.013$ between genders). Upon frowning, the distance between the crease and the midline was 4.32 [1.6] mm (range, 2.0-9.8 mm) in males and 5.16 [1.7] mm (range, 2.6-10.7 mm) in females ($P = 0.019$ between genders). The difference in position of the crease between rest and frowning was 1.3 mm in males ($P < 0.001$) and 1.4 mm in females ($P < 0.001$). This indicates a highly statistically significant medial shift of the crease directed towards the midline when frowning, independent of gender.

Distance of Arteries from the Midline

The mean distance at rest between the supratrochlear artery and the midline was 16.13 [3.8] mm (range, 6.0-23.0) for males and 14.80 [3.5] mm (range, 6.0-21.0 mm) for females ($P = 0.099$ between genders). None (0%) of the supratrochlear arteries were located within 5 mm of the midline, 7.3% were between 6 and 10 mm from the midline, 36.6% between 11 and 15 mm, 45.1% between 16 and 20 mm, and 11.0% between 21 and 25 mm (Figure 2). Upon frowning, the mean distance of the supratrochlear artery from the midline was 13.27 [3.3] mm (range, 5.4-19.7 mm) in males and 11.53 [2.7] mm (range, 4.40-15.5) in females ($P = 0.010$ between genders). The difference in distance to the midline between the 2 different facial expressions (rest vs frowning) was 2.9 mm in males ($P < 0.001$) and 3.3 mm in females ($P < 0.001$), indicating a statistically significant medial shift in arterial position in both genders upon frowning (Figure 3).

The supraorbital artery had a mean distance to the midline at rest of 27.93 [5.3] mm (range, 15.3-36.9 mm) in males and

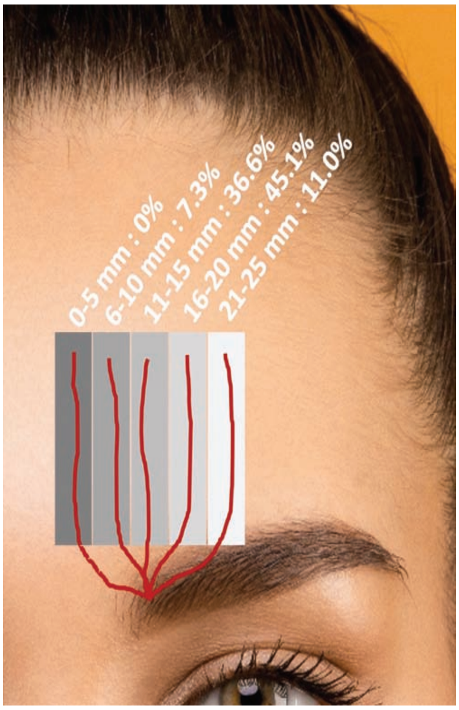

Figure 2. Schematic photograph of a 22-year-old female showing the distribution of the supratrochlear artery in the respective area as a percentage in relation to the midline. Note that the supratrochlear artery could not be found within 0 to 5 mm lateral of the midline and could be found most frequently between 16 and 20 mm.

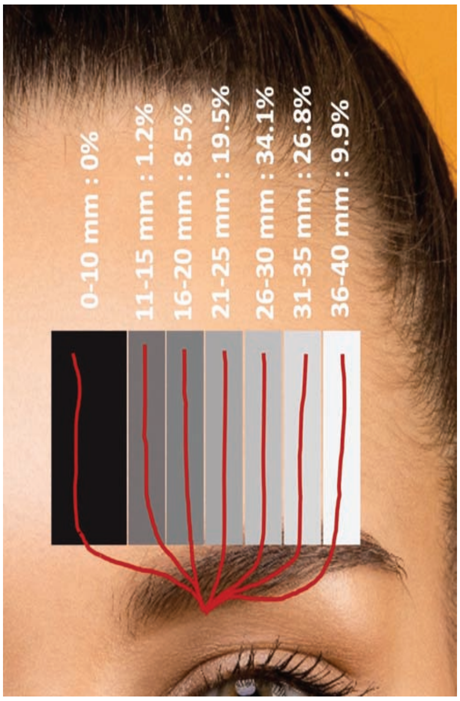

Figure 4. Schematic photograph of a 22-year-old female showing the distribution of the supraorbital artery in the respective area as a percentage in relation to the midline. Note that the supraorbital artery could not be found within 0 to 15 mm lateral of the midline and could be found most frequently between 26 and 30 mm.

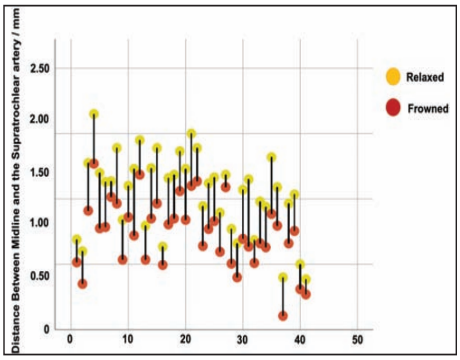

Figure 3. Scatter-dot showing the distance (mm) between the midline and the superficial branch of the supratrochlear artery for each participant as the subjects change from relaxed (yellow dot) to frowning (red dots).

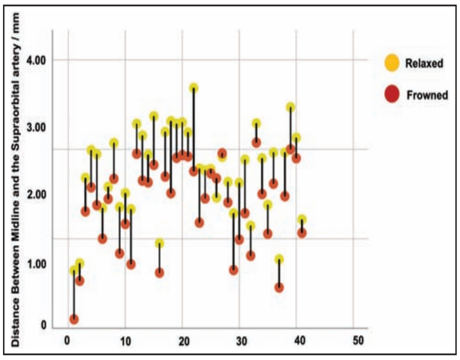

Figure 5. Scatter-dot showing the distance (mm) between the midline and the deep branch of the supraorbital artery for each participant as the subjects change from relaxed (yellow dot) to frowning (red dots).

27.31 [5.9] mm (range, 13.8-39.1 mm) in females ($P = 0.623$ between genders). None (0%) of the supraorbital arteries were located within 10 mm of the midline, 1.2% were between 11 and 15 mm from the midline, 8.5% between 16 and 20 mm, 19.5% between 21 and 25 mm, 34.1% between 26 and 30 mm, 26.8% between 31 and 35 mm, and 9.9% between 36 and 40 mm (Figure 4). Upon frowning, the mean distance of the supraorbital artery from the midline was 24.08 [5.5] mm (range, 8.8-31.8 mm) in males and 23.44 [5.4] mm (range, 14.0-32.2 mm) in females (P = 0.598 between genders). No differences between sides were detected. Frowning caused a medial shift in supraorbital arterial position of 3.9 mm in both males and females (P < 0.001 for both genders) (Figure 5).

Relation Between Supratrochlear Artery and Vertical Glabellar Line

The mean distance between the supratrochlear artery and the ipsilateral vertical glabellar frown line at rest was 10.59 [4.0] mm (range, 2.9-19.0 mm) in males and 8.21 [4.0] mm (range, –3.3 to 14.2 mm) in females (P = 0.009 between genders). In one single case (n = 1), the distance between the vertical glabellar line and the supratrochlear artery was only 0.9 mm.

The distance between the crease and the artery when frowning was 8.96 [3.5] mm (range, 2.3-17.0 mm) in males and 6.37 [3.3] mm (range, –2.8 to 12.1 mm) in females (P = 0.001 between genders). Upon frowning, the medial shift in supratrochlear arterial position was 1.63 mm in males (P < 0.001) and 1.84 mm in females (P < 0.001). The shift in arterial position always occurred towards the glabellar crease regardless of whether the artery started out medial (n = 1, from 3.3 to 2.8 mm) or lateral to the crease (n = 81 measurements per side, from 9.5 to 7.8 mm).

Relation Between Supraorbital Artery and Vertical Glabellar Line

The mean distance between the supraorbital artery and the ipsilateral vertical glabellar frown line at rest was 22.38 [5.5] mm (range, 6.8-31.1 mm) in males and 20.73 [5.6] mm (range, 6.2-28.8 mm) in females, without statistically significant difference between genders and side.

Upon frowning, the mean distance to the ipsilateral vertical glabellar line was 19.76 [5.6] mm (range, 2.8-29.1 mm) in males and 18.28 [5.4] mm (range, 7.1-27.2 mm) in females, without statistically significant difference between genders and side. In males, the artery shifted medially by a mean value of 2.6 mm (P < 0.001) whereas in females the artery shifted medially by 2.5 mm (P < 0.001).

DISCUSSION

Bilateral, ultrasound-based measurements of the supraorbital area were conducted in 41 healthy, aesthetic-procedure-naive volunteers.

The results of this investigation revealed that the soft tissues of the glabellar region should be considered as a mobile entity rather than a static one. Due to the muscular contraction of (primarily) the corrugator supercilii muscle the glabellar soft tissues are displaced medially. This is indicated by the medial shift of the vertical glabellar line by 1.3 mm in males and by 1.4 mm in females. This leads to an overall highly statistically significant medial displacement of both the supratrochlear (males, 2.9 mm; females, 3.3 mm) and supraorbital arteries (3.9 mm for both males and females), when measured from the midline. Relating these movements to the ipsilateral vertical glabellar line, it was, however, identified that if the supratrochlear artery was located medial to the crease, the movement was directed laterally (ie, towards the crease), whereas if the supratrochlear artery was located lateral to the crease the movement was directed medially (ie, towards the crease). This is plausible as the formation of the crease is predominantly caused by the direction and the magnitude of the contraction of the corrugator supercilii muscle, which causes an antagonistic soft-tissue movement pattern between soft tissues medial vs lateral to the crease. This is supported by the measured change in distances of the supratrochlear artery in relation to the crease: medial to the crease from 3.3 to 2.8 mm vs lateral to the crease from 9.5 to 7.8 mm. The supraorbital artery had a mean distance to the ipsilateral vertical glabellar line of 22.38 [5.5] in males and of 20.73 [5.6] mm in females and those distances reduced upon contraction by 2.6 mm in males and by 2.5 mm in females.

From the clinical perspective this is of importance because estimating the 2-dimensional (2D) course of the supratrochlear and supraorbital vasculature is crucial to avoid adverse vascular events when injecting soft tissue fillers, especially when utilizing needles in the supraorbital region.[5,6,10,15,16] Taking the general landmark supraorbital foramen as delineating the course of the supraorbital artery and the medial limbus as delineating the course of the supratrochlear artery might prove to be inaccurate if a highly contracted glabella is present. In this case the increased muscular tone might tend to displace the arteries medially, making it more difficult to estimate the course of the arteries and safely administer soft tissue fillers. Administering neuromodulators first could reposition the supratrochlear/supraorbital arteries and estimates of their 2D course might become more predictable.

Previous investigations have indicated that skin wrinkles are closely associated with the presence of lymphatic and arterial vessels.[17] In the glabellar region, it was additionally postulated that the vertical glabellar lines can be used as a reliable landmark to harvest the supratrochlear vascular pedicle for the paramedian forehead flap if Doppler ultrasound imaging is not helpful.[13] In their study Vural et al[13] reported that the superficial branch of the supratrochlear artery coursed immediately inferior to the crease in 49% of the investigated volunteers. This resulted in the assumption that injecting soft tissue filler deep to the vertical glabellar lines might result in an increased risk of intra-arterial application of the injected material.[17] Intra-arterial applications of soft tissue fillers into the superficial branch of the supratrochlear artery have been recently shown to be associated with injection-related visual compromise[9] as the material can be transported to the ophthalmic artery circulation, causing irreversible blindness by embolizing retinal arteries.[8]

The results of the present study, however, show a less close association between the pathway of the superficial branch of the supratrochlear artery and the vertical glabellar lines. The mean lateral distance of the artery to the crease was 10.59 [4.0] mm in males and 8.21 [4.0] mm in females. In 98.8% of the cases the artery was greater than 1 mm from the ipsilateral vertical glabellar line. This is of great clinical importance as it implies that the association between the crease and artery must be re-evaluated. The hypothesis that injecting next to the vertical glabellar line is safe because the artery courses at the location of the crease should be rejected. Furthermore, the glabella as an aesthetic region should be regarded as a high-risk zone for causing injection-related visual compromise because the course of the arteries is not predictable in their 2D pathway because the location of the artery changes with contraction of the muscles in this region.[8,14] This is supported by reports on the incidence of irreversible blindness: the glabella is ranked amongst the areas with the highest incidence when compared to all facial regions.[5,6]

The depth of the arteries was 3.34 [0.6] mm for the supratrochlear artery and 3.54 [0.8] mm for the supraorbital artery when measured from the skin surface at the horizontal mid-eyebrow level. Increased BMI significantly influenced the depth of the supraorbital artery (increase in distance with increased BMI) but not the depth of the supratrochlear artery. Clinically, this indicates that the supratrochlear artery might have a more stable depth when related to the skin surface, which is supported by the smaller data range (3.3 mm) as opposed to a data range of 4.5 mm for the supraorbital artery across the sample investigated in this study.

The strengths of this investigation are the gender-balanced study population with n = 20 males and n = 21 females and the young age of the subjects (mean age, 26.17 years). This allows conclusions to be drawn about normal glabellar and supraorbital vascular and soft tissue anatomy which is not (yet) affected by advanced age-related changes. This sample is additionally a good representation of patients seeking aesthetic treatments on a daily basis which supports the extrapolation of the findings presented herein to the greater population. Another strength of this study is the noninvasive nature of the ultrasound measurements performed. Real-time measurements were obtained without skin contact or application of pressure (ie, sound waves were transmitted via the visualization gel), preserving the original tissue thickness. However, the applied methodology can also be regarded as a limitation of this study because ultrasound-based measurements are subject to observer bias and might have a low reproducibility if performed by another investigator. To ensure consistency throughout all measurements performed in this study, one single investigator conducted the scans and performed all measurements to reduce this bias (ICC, 0.938).

Another limitation of the study is the small sample size (n = 41); a larger study population could have provided a more robust data set. Future studies might need to validate and/or expand the results presented herein and should additionally include volunteers from different ethnic populations and various age groups.

CONCLUSIONS

The hypothesis that injecting soft tissue fillers adjacent to vertical glabellar lines is safe because the artery courses deep to the crease should be rejected based on the results of this study. The superficial branch of the supratrochlear artery courses on average 10 mm lateral to the crease in males and 8 mm in females. Thus, injecting soft tissue fillers adjacent to the glabellar crease rather than deep to it does not necessarily reduce the risk of intravascular injection and, in fact, may be more dangerous. Additionally, the glabella and the supraorbital region should be considered as an area of mobile rather than static soft tissues. Taking this mobility into account could guide treatment sequences (eg, applying neuromodulator first) and increase safety when injecting the glabella/supraorbital area for aesthetic purposes with soft tissue fillers.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. The American Society for Aesthetic Plastic Surgery's Cosmetic Surgery National Data Bank: statistics 2018. *Aesthet Surg J.* 2019;39(Suppl_4):1-27.
2. Casabona G, Frank K, Koban KC, et al. Lifting vs volumizing—the difference in facial minimally invasive procedures when respecting the line of ligaments. *J Cosmet Dermatol*. 2019. doi: 10.1111/jocd.13089. [Epub ahead of print]
3. Schenck TL, Koban KC, Schlattau A, et al. The functional anatomy of the superficial fat compartments of the face: a detailed imaging study. *Plast Reconstr Surg.* 2018;141(6):1351-1359.

4. Cotofana S, Gotkin RH, Morozov SP, et al. The relationship between bone remodeling and the clockwise rotation of the facial skeleton: a computed tomographic imaging-based evaluation. *Plast Reconstr Surg.* 2018;142(6):1447-1454.
5. Beleznay K, Carruthers JDA, Humphrey S, Jones D. Avoiding and treating blindness from fillers. *Dermatologic Surg*. 2015;41(10):1097-1117.
6. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, Jones D. Update on avoiding and treating blindness from fillers: a recent review of the world literature. *Aesthet Surg J.* 2019;39(6):662-674.
7. Frank K, Koban K, Targosinski S, et al. The anatomy behind adverse events in hand volumizing procedures: retrospective evaluations of 11 years of experience. *Plast Reconstr Surg.* 2018;141(5):650e-662e.
8. Cotofana S, Lachman N. Arteries of the face and their relevance for minimally invasive facial procedures: an anatomical review. *Plast Reconstr Surg.* 2019;143(2):416-426.
9. Cho KH, Dalla Pozza E, Toth G, Bassiri Gharb B, Zins JE. Pathophysiology study of filler-induced blindness. *Aesthet Surg J.* 2019;39(1):96-106.
10. Pavicic T, Frank K, Erlbacher K, et al. Precision in dermal filling: a comparison between needle and cannula when using soft tissue fillers. *J Drugs Dermatol.* 2017;16(9):866-872.
11. Pavicic T, Yankova M, Schenck TL, et al. Subperiosteal injections during facial soft tissue filler injections—is it possible? *J Cosmet Dermatol.* 2020;19(3):590-595.
12. Sykes JM, Cotofana S, Trevidic P, et al. Upper face: clinical anatomy and regional approaches with injectable fillers. *Plast Reconstr Surg*. 2015;136(5 Suppl):204S-218S.
13. Vural E, Batay F, Key JM. Glabellar frown lines as a reliable landmark for the supratrochlear artery. *Otolaryngol Head Neck Surg.* 2000;123(5):543-546.
14. Cong LY, Phothong W, Lee SH, et al. Topographic analysis of the supratrochlear artery and the supraorbital artery: implication for improving the safety of forehead augmentation. *Plast Reconstr Surg.* 2017;139(3):620e-627e.
15. Pavicic T, Webb KL, Frank K, Gotkin RH, Tamura B, Cotofana S. Arterial wall penetration forces in needles versus cannulas. *Plast Reconstr Surg.* 2019;143(3):504e-512e.
16. Pavicic T, Yankova M, Schenck TL, et al. Subperiosteal injections during facial soft tissue filler injections—is it possible? *J Cosmet Dermatol.* 2020;19(3):590-595.
17. Pessa JE, Nguyen H, John GB, Scherer PE. The anatomical basis for wrinkles. *Aesthet Surg J.* 2014;34(2):227-234.

7. Veröffentlichung III

Original Research

Performing Distance Measurements in Curved Facial Regions: A Comparison between Three-Dimensional Surface Scanning and Ultrasound Imaging

Michael Alfertshofer[1] Konstantin Frank, MD[1] Dmitry V. Melnikov, MD[2] Nicholas Möllhoff, MD[1] Robert H. Gotkin, MD[3] David Lysander Freytag, MD[1] Stephan Heisinger, MD[4] Riccardo E. Giunta, MD, PhD[1] Thilo L. Schenck, MD, PhD[1] Sebastian Cotofana, MD, PhD[5]

[1] Department of Hand, Plastic and Aesthetic Surgery, Ludwig-Maximilian University, Munich, Germany
[2] Plastic Surgery Department, I. M. Sechenov First Moscow State Medical University, Moscow, Russia
[3] Private Practice, New York City, New York
[4] Department of Orthopedics and Trauma Surgery, Medical University of Vienna, Wien, Austria
[5] Department of Medical Education, Albany Medical College, Albany, New York

Address for correspondence Konstantin Frank, MD, Department of Hand, Plastic and Aesthetic Surgery, Ludwig-Maximilian University, Pettenkoferstraße 8a, Munich 80336, Germany (e-mail: konstantinfrank@me.com).

Facial Plast Surg

Abstract

Facial flap surgery depends strongly on thorough preoperative planning and precise surgical performance. To increase the dimensional accuracy of transferred facial flaps, the methods of ultrasound and three-dimensional (3D) surface scanning offer great possibilities. This study aimed to compare different methods of measuring distances in the facial region and where they can be used reliably. The study population consisted of 20 volunteers (10 males and 10 females) with a mean age of 26.7 ± 7.2 years and a mean body mass index of 22.6 ± 2.2 kg/m^2. Adhesives with a standardized length of 20 mm were measured in various facial regions through ultrasound and 3D surface scans, and the results were compared. Regardless of the facial region, the mean length measured through ultrasound was 18.83 mm, whereas it was 19.89 mm for 3D surface scans, with both $p < 0.0001$. Thus, the mean difference was 1.17 mm for ultrasound measurements and 0.11 mm for 3D surface scans. Curved facial regions show a great complexity when it comes to measuring distances due to the concavity and convexity of the face. Distance measurements through 3D surface scanning showed more accurate distances than the ultrasound measurement. Especially in “complex” facial regions (e.g., glabella region and labiomental sulcus), the 3D surface scanning showed clear advantages.

Keywords
- ultrasound imaging
- 3D surface scanning
- facial anatomy
- facial analysis

A total of 4.5 million tumor removal procedures were performed by plastic surgeons in the United States in the year 2019.[1] While some of the defects resulting from such tumor extirpation can be closed by simple, intermediate, or complex repair, a large number result in tissue deficits that require flap reconstruction.[2–6] Flap design depends on a plethora of factors; however, initial surgical planning always needs to ensure proper vascularization and blood supply of the flap.[7] Ultrasound imaging is a commonly used tool to visualize the course of vessels prior to surgery and to facilitate the planning

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0041-1725166.
ISSN 0736-6825.

of more complex reconstructive surgery. Ultrasound-based imaging has been shown to be cost-effective, fast, readily available, and radiation-free, as compared with computed tomography (CT).[8] Proper visualization of perforators can diminish the risk of postoperative wound-healing disturbances or skin necrosis by ensuring proper vascularization of a flap.[8]

While identification of perforators using ultrasound imaging is widely established and has mainly displaced classical audio-based Doppler ultrasound detection of perforators, in the field of complex facial and nasal reconstruction (postextirpative or otherwise), courses of entire vessels might need to be identified. However, surgeons often rely on the proper measurement of distances, lengths, and relations of the vessel along their course. Apart from identifying proper vascularization, proper distance measuring and preoperative simulation is key to a successful reconstruction. Three-dimensional (3D) surface scanning has been shown to be a helpful tool in the planning of breast surgery and facial surgery.[9–13] Both entities can be combined: ultrasound imaging can be used to visualize and measure structures *beneath* the skin, whereas 3D surface scanning can be used to evaluate the surface itself.

However, when planning vascularized flaps for complex facial reconstruction, the location and course of the facial vasculature need to be accurately evaluated preoperatively, and planning should include information both on the superficial and deep facial vasculature. This study was designed to investigate whether 3D surface scanning or ultrasound imaging provides reliable distance measurements in curved facial regions when compared with a known standard reference.

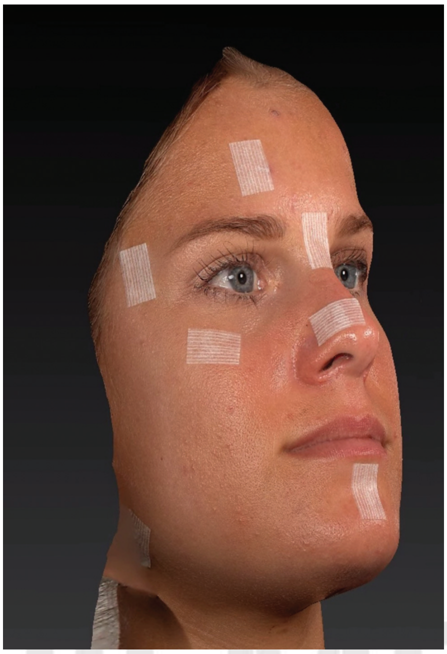

Fig. 1 Placement of all facial adhesives during the study. The adhesives were placed in the frontal region, in the glabella region, on the lateral orbital rim, on the zygomatic arch, on the nose tip, on the mandibular angle, and in the mental region.

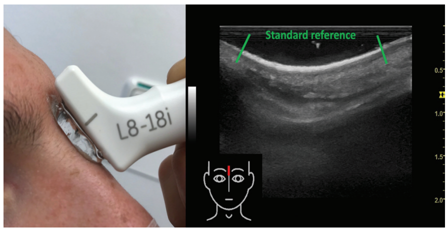

Fig. 2 Measurement methodology in the concave glabella region. To avoid compression to the underlying tissue, enough ultrasound visualization gel was used for the distance measurements of the adhesive.

Materials and Methods

Sample Size

The study investigated a total of 20 healthy volunteers (10 males and 10 females) of Caucasian ethnicity with a mean age of 26.7 ± 7.2 years (range: 22–54 years) and a mean body mass index of 22.6 ± 2.2 kg/m^2 (range: 18.2–26.0 kg/m^2). Volunteers were recruited from the Department of Hand, Plastic and Aesthetic Surgery, Ludwig-Maximilian University, Munich, Germany.

This study was performed in adherence with the Declaration of Helsinki (1996)[14] and was previously approved by the Ethics Committee of the Ludwig-Maximilian University under the number: 19–999. Written informed consent was obtained from all participants for the use of their facial images and personal data for research purposes and publication prior to inclusion in the study.

Study Design

The study used a defined standard reference in the form of a 20-mm-long facial adhesive (R1547 Steri-Strip, 3M Deutschland GmbH, Neuss, Germany) to compare differences in length measurements performed by 3D surface scanning and by ultrasound imaging.

The standard reference was placed at seven different facial regions (unilateral): forehead, glabella, lateral orbital rim, tip of the nose, malar eminence, labiomental sulcus, and mandibular angle (►**Fig. 1**).

Three-Dimensional Surface Scanning

After the standard reference was placed on each facial region of interest, the faces of the 20 volunteers were scanned in an upright standing position using a Vectra X3 camera (Canfield Scientific Inc., Fairfield, NJ). The generated images were imported into the proprietary Vectra Software Suite (Canfield Scientific Inc.), and the length of the standard reference of each facial region was measured with the internal software measurement tools (►**Fig. 2**). All surface analytic procedures were conducted by the same investigator (M.G.A.).

Ultrasound Imaging

Each facial region containing the standard reference was investigated through ultrasound imaging using an 18-MHz

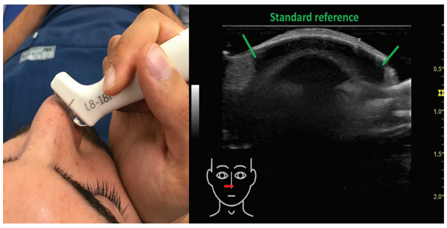

Fig. 3 Measurement methodology on the convex nose tip. To avoid compression to the underlying tissue, enough visualization gel was used for the distance measurements of the adhesive.

linear transducer (LOGIQ S7 Expert, GE Healthcare GmbH, Solingen, Germany). All study participants were scanned in an upright seated position. The respective facial region of interest was covered in sufficient ultrasound contact gel (Aquasonic Clear Ultrasound Gel, Parker Laboratories Inc., Fairfield, NJ) to enable measurement of the complete length of the standard reference without skin contact (►**Fig. 3**). Length measurements were conducted through the internal measurement software of the ultrasound device and performed by the same investigator to assure consistency throughout the measurements (M.G.A.). The interclass correlation coefficient for facial ultrasound measurements of the investigator was previously determined with intraclass correlation coefficient = 0.938.[15]

Statistical Analysis

The difference to the true length of the standard reference was calculated for each of the measurement modalities (3D surface scanning vs. ultrasound imaging) and compared using a paired Student's *t*-test. Analyses were performed using SPSS Statistics version 23 (IBM, Armonk, NY), and differences were considered statistically significant at a probability level of ≤ 0.05 to guide conclusions.

Results

Overall Difference

The mean overall difference to the standard reference (= 20.00 mm), independent of the facial region, was 0.11 (0.1) mm for the 3D measurements, whereas it was 1.17 (0.3) mm for the ultrasound measurements; this represents a highly statistically significant difference in measurement accuracy between the two modalities with $p < 0.001$. All measurements conducted were smaller than the standard reference; none of the conducted measurements overestimated the length of the standard reference. The greatest difference was observed at the labiomental sulcus for measurements conducted with ultrasound imaging and at the tip of the nose for 3D surface scanning. The smallest difference was observed for both procedures at the orbital rim.

Forehead Measurements

The mean difference to the standard reference was 0.65 (0.4) mm conducting ultrasound imaging and 0.06 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the forehead.

Glabella Measurements

The mean difference to the standard reference was 1.49 (0.5) mm conducting ultrasound imaging and 0.12 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the glabella.

Lateral Orbital Rim Measurements

The mean difference to the standard reference was 0.56 (0.3) mm conducting ultrasound imaging and 0.03 (0.1) mm conducting 3D surface scanning, with $p < 0.001$ at the lateral orbital rim.

Tip of the Nose Measurements

The mean difference to the standard reference was 1.90 (0.7) mm conducting ultrasound imaging and 0.26 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the tip of the nose.

Malar Eminence Measurements

The mean difference to the standard reference was 0.80 (0.4) mm conducting ultrasound imaging and 0.11 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the malar eminence.

Labiomental Sulcus Measurements

The mean difference to the standard reference was 2.01 (0.8) mm conducting ultrasound imaging and 0.12 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the labiomental sulcus.

Mandibular Angle Measurements

The mean difference to the standard reference was 0.73 (0.4) mm conducting ultrasound imaging and 0.08 (0.2) mm conducting 3D surface scanning, with $p < 0.001$ at the mandibular angle.

Discussion

This study investigated the measurement error of ultrasound imaging and 3D surface scanning in various curved facial regions compared with a standard reference. Overall, both imaging modalities underestimated the length of the standard reference of 20 mm, with ultrasound imaging having a mean difference of 1.17 mm (18.83 mm; $p < 0.001$) and 3D surface scanning having a mean difference of 0.11 mm (19.89 mm; $p < 0.001$). The difference to the standard reference of both imaging modalities was highly statistically significant with $p < 0.001$ in the investigated sample of 20 patients; with seven investigated facial regions per patient, this resulted in a total of 140 conducted comparisons.

The results of this study confirmed the limited ability of both imaging modalities to accurately measure distances on the skin surface, especially for curved facial regions. While ultrasound imaging had a range in measurement error between 0.03 to 1.64 mm, 3D surface scanning had a range of –0.04 to 0.31mm independent of the measured facial region. Curved facial regions pose a substantial difficulty for linear distance measurement systems such as ultrasound imaging. The manual caliper-based measures in ultrasound imaging rely on linear distance measurements, which do not recognize the curve of a given surface. The internal measurement algorithm is generally aligned to calculate the linear and direct distance between the two manually positioned calipers irrespective of the surface characteristics. For curved surfaces, it is plausible that the actual length of a standard reference on the skin surface is *underestimated* due to the measurement algorithm. The results of this study confirm this underestimation; the ultrasound imaging derived measurements were, on average, 18.83 mm versus 20 mm of the standard reference.

The greatest difference to the standard reference for ultrasound imaging was detected in the labiomental sulcus with a mean difference of 2.0 1mm. This can be easily explained and understood because the sulcus between the lower lip and the mental prominence can be deep and acute. The second location where ultrasound imaging showed its greatest difficulties in accuracy was the nose, with a mean difference to the standard reference of 1.90 mm. Here, likewise, the curve of the surface is substantial, and linear distance measurements are the least reliable.

The methodology applied during ultrasound imaging to best accommodate for curved surfaces included the usage of a substantial amount of contact gel to visualize the total length of the standard reference (►**Figs. 3** and **4**). A limited amount of contact gel would reduce the visibility of the margins of the standard reference and this would result in more inaccurate measurements. Additionally, using large amounts of contact gel allows one to position the transducer exclusively into the gel without skin contact. Limiting skin contact minimizes the possibility of surface compression by the transducer and allows more accurate surface length measurements. Additionally, as described in previous studies,[16–20] having no contact between the skin surface and the transducer is of crucial importance when measuring soft tissue thickness or the depth of neurovascular structures.

Three-dimensional surface scanning, performed with a Vectra X3 camera, resulted in a statistically significant

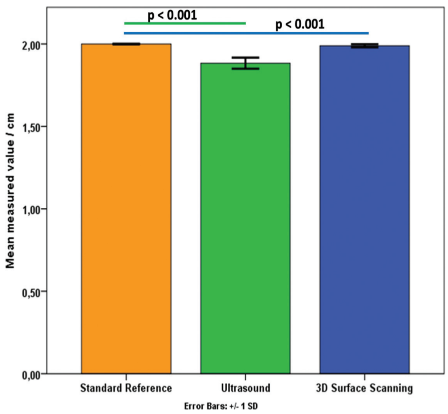

Fig. 4 Overview: measurement accuracy of ultrasound and three-dimensional scan measurements compared with a standardized length of 20 mm of the adhesive.

improvement in the accuracy of the length measurements compared with ultrasound imaging, with $p < 0.001$ for all investigated facial regions. The average value across all facial regions was 19.89 versus 20 mm of the standard reference. This is most likely due to the measurement modality of 3D surface scanning, which better recognizes curved surfaces and other surface characteristics. As opposed to ultrasound imaging, the 3D surface scanning measurements are not based on manual caliper placement but on the digital measurements of surface contours. This would explain the lower average difference of 0.11 mm to the standard reference. Similar to the results with ultrasound imaging, greater differences were detected for the nose (0.26 mm) and for the glabella and labiomental sulcus (both with 0.12 mm).

For clinical applications, the results of this study indicate that surface distance measurements, especially in curved facial regions, should be performed with 3D surface scanning rather than with ultrasound imaging. The measurements performed revealed that using ultrasound imaging results in the underestimation of length measurements that follow surface contours. This could create a similar underestimation in length measurements when planning facial flaps during various surgical procedures. A tensionless apposition of neurovascular structures and skin is crucial for the surgical outcome and should be planned with greatest accuracy as possible.[21,22] Using ultrasound imaging for these purposes in facial regions with curved surfaces, such as the nose or the lower lip, should be conducted with caution, and surgeons should account for the bias in length measurements. However, it must be noted that 3D surface scanning is costly, and the analyses require a certain training and learning phase as they are not intuitive compared with ultrasound imaging. This could be a disadvantage when trying to implement such technology in the daily clinical routine. However, if 3D surface scanning and ultrasound imaging are both available, marking the vessel on the skin using ultrasound and performing additive measurements using 3D surface imaging blends both technologies to better detect the depth of structures beneath the skin surface and uses the greater reliability of distance measurements with 3D surface imaging.

The results of this study are in line with a previous study, which investigated a similar 3D surface scanning system and compared manual versus 3D surface scanning in patients with cleft lip and palate.[23] The error margin for distance measurements reported in that study was within a range of ±2 mm; this is higher than the results presented herein (0.0–0.3 mm). Similar to our study, the authors concluded that it is a suitable clinical application of the 3D surface scanning system, but they also pointed out that training of an operator who can support image analysis and image distance measurements is strictly advisable.

Conclusion

The results of this study revealed that distance measurements performed in curved facial regions are more accurate compared with a standard reference when performed with 3D surface scanning than with ultrasound imaging. Both methodologies underestimate the real value, and this difference can be attributed to the measuring method: linear in ultrasound and surface-dependent in 3D surface scanning. Surgical planning of complex, composite facial flaps where tensionless skin and/or neurovascular apposition is mandatory for the best surgical outcome should, therefore, rely on the more accurate 3D surface scanning procedures.

Conflict of Interest
None declared.

References

1 American Society of Plastic Surgeons. Plastic Surgery Statistics Report. Accessed August 15, 2020 at: https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics-full-report-2019.pdf
2 Ehrl D, Rentsch M, Moellhoff N, Wachtel N. Complex microsurgical perineal reconstruction after resection of a giant verrucous carcinoma associated with anal fistulas in Crohn's disease-a unique case report. Int J Colorectal Dis 2020;35(07):1337–1341
3 Ehrl D, Brueggemann A, Broer PN, Koban K, Giunta R, Thon N. Scalp reconstruction after malignant tumor resection: an analysis and algorithm. J Neurol Surg B Skull Base 2020;81(02):149–157
4 Ehrl D, Heidekrueger PI, Schmitt A, et al. The anterolateral thigh flap for Achilles tendon reconstruction: functional outcomes. Plast Reconstr Surg 2019;143(06):1772–1783
5 Broer PN, Moellhoff N, Mayer JM, Heidekrueger PI, Ninkovic M, Ehrl D. Comparison of outcomes of end-to-end versus end-to-side anastomoses in lower extremity free flap reconstructions. J Reconstr Microsurg 2020;36(06):432–437
6 Prantl L, Moellhoff N, Fritschen UV, et al. Impact of smoking status in free deep inferior epigastric artery perforator flap breast reconstruction: a multicenter study. J Reconstr Microsurg 2020; 36(09):694–702
7 Behan FC. The keystone design perforator island flap in reconstructive surgery. ANZ J Surg 2003;73(03):112–120
8 Homsy C, McCarthy ME, Lim S, Lindsey JT Jr, Sands TT, Lindsey JT Sr. Portable color-flow ultrasound facilitates precision flap planning and perforator selection in reconstructive plastic surgery. Ann Plast Surg 2020;84(6S, Suppl 5):S424–S430
9 Koban KC, Cotofana S, Frank K, et al. Precision in 3-dimensional surface imaging of the face: a handheld scanner comparison performed in a cadaveric model. Aesthet Surg J 2019;39(04): NP36–NP44
10 Cotofana S, Koban K, Pavicic T, et al. Clinical validation of the surface volume coefficient for minimally invasive treatment of the temple. J Drugs Dermatol 2019;18(06):533
11 Koban KC, Härtnagl F, Titze V, Schenck TL, Giunta RE. Chances and limitations of a low-cost mobile 3D scanner for breast imaging in comparison to an established 3D photogrammetric system. J Plast Reconstr Aesthet Surg 2018;71(10):1417–1423
12 Koban KC, Leitsch S, Holzbach T, Volkmer E, Metz PM, Giunta RE. 3D Bilderfassung und Analyse in der Plastischen Chirurgie mit Smartphone und Tablet: eine Alternative zu professionellen Systemen? Handchir Mikrochir Plast Chir 2014;46(02):97–104
13 Koban KC, Frank K, Etzel L, Schenck TL, Giunta RE. 3D mammometric changes in the treatment of idiopathic gynecomastia. Aesthetic Plast Surg 2019;43(03):616–624
14 World Medical Association. WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Accessed August 5, 2018 at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
15 Cotofana S, Alfertshofer M, Schenck TL, et al. Anatomy of the superior and inferior labial arteries revised: an ultrasound investigation and implication for lip volumization. Aesthet Surg J 2020: sjaa137
16 Cotofana S, Hexsel D, Avelar LET, et al. Calculating the thickness of the superficial fatty layer of the body using age, gender, and body mass index. J Drugs Dermatol 2020;19(01):36–44
17 Casabona G, Frank K, Koban KC, et al. Influence of age, sex, and body mass index on the depth of the superficial fascia in the face and neck. Dermatol Surg 2019;45(11):1365–1373
18 Casabona G, Frank K, Koban KC, et al. Influences of age, gender, and body mass index on the depth of the superficial fascia of the arm and thigh. Dermatol Surg 2019 (e-pub ahead of print). . Doi: 10.1097/DSS.0000000000001986
19 Frank K, Hamade H, Casabona G, et al. Influences of age, gender, and body mass index on the thickness of the abdominal fatty layers and its relevance for abdominal liposuction and abdominoplasty. Aesthet Surg J 2019;39(10):1085–1093
20 Frank K, Casabona G, Gotkin RH, et al. Influence of age, sex, and body mass index on the thickness of the gluteal subcutaneous fat: implications for safe buttock augmentation procedures. Plast Reconstr Surg 2019;144(01):83–92
21 Frank K, Englbrecht M, Koban KC, et al. Nerve transfer of the anterior interosseous nerve to the thenar branch of the median nerve - an anatomical and histological analysis. J Plast Reconstr Aesthet Surg 2019;72(05):751–758
22 Lockwood T. High-lateral-tension abdominoplasty with superficial fascial system suspension. Plast Reconstr Surg 1995;96(03):603–615
23 Othman SA, Saffai L, Wan Hassan WN. Validity and reproducibility of the 3D VECTRA photogrammetric surface imaging system for the maxillofacial anthropometric measurement on cleft patients. Clin Oral Investig 2020;24(08):2853–2866

8. Literaturverzeichnis

1. International Society of Aesthetic Plastic Surgeons. *ISAPS International Survey on Aesthetic/Cosmetic Procedures Performed in 2017.*; 2019. https://www.isaps.org/wp-content/uploads/2019/03/ISAPS_2017_International_Study_Cosmetic_Procedures_NEW.pdf
2. Little AC, Jones BC, DeBruine LM. Facial attractiveness: evolutionary based research. *Philos Trans R Soc London Ser B, Biol Sci*. 2011;366(1571):1638-1659. doi:10.1098/rstb.2010.0404
3. Zebrowitz LA, Montepare JM. Social Psychological Face Perception: Why Appearance Matters. *Soc Personal Psychol Compass*. 2008;2(3):1497. doi:10.1111/j.1751-9004.2008.00109.x
4. Devgan L, Singh P, Durairaj K. Minimally Invasive Facial Cosmetic Procedures. *Otolaryngol Clin North Am*. 2019;52(3):443-459. doi:10.1016/j.otc.2019.02.013
5. de Melo F, Carrijo A, Hong K, et al. Minimally Invasive Aesthetic Treatment of the Face and Neck Using Combinations of a PCL-Based Collagen Stimulator, PLLA/PLGA Suspension Sutures, and Cross-Linked Hyaluronic Acid. *Clin Cosmet Investig Dermatol*. 2020;13:333-344. doi:10.2147/CCID.S248280
6. Werschler WP, Calkin JM, Laub DA, Mauricio T, Narurkar VA, Rich P. Aesthetic Dermatologic Treatments: Consensus from the Experts. *J Clin Aesthet Dermatol*. 2015;8(10 Suppl):S2-7.
7. ASPS National CLearinghouse of Plastic Surgery Procedural Statistics. Plastic Surgery Statistics Report 2019. Published online 2019:1-25. https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics-full-report-2019.pdf
8. Wollina, Goldman. Minimally invasive aesthetic procedures in young adults. *Clin Cosmet Investig Dermatol*. 2011;(May):19. doi:10.2147/ccid.s17467
9. Ogden S, Griffiths TW. A review of minimally invasive cosmetic procedures. *Br J Dermatol*. 2008;159(5):1036-1050. doi:10.1111/j.1365-2133.2008.08845.x
10. de Maio M. The minimal approach: an innovation in facial cosmetic procedures. *Aesthetic Plast Surg*. 2004;28(5):295-300. doi:10.1007/s00266-004-0037-1
11. Sturm LP, Cooter RD, Mutimer KL, Graham JC, Maddern GJ. A systematic review of dermal fillers for age-related lines and wrinkles. *ANZ J Surg*. 2011;81(1-2):9-17. doi:10.1111/j.1445-2197.2010.05351.x
12. C.M. B. Principles of soft tissue augmentation for the aging face. *Clin Interv Aging*. 2006;1(4):349-355. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L350325504
13. Jones D. Volumizing the Face With Soft Tissue Fillers. *Clin Plast Surg*. 2011;38(3):379-390. doi:10.1016/j.cps.2011.03.011
14. Jagdeo J, Ho D, Lo A, Carruthers A. A systematic review of filler agents for aesthetic treatment of HIV facial lipoatrophy (FLA). *J Am Acad Dermatol*. 2015;73(6):1040-1054.e14. doi:10.1016/j.jaad.2015.08.040
15. Oxlund H, Andreassen TT. The roles of hyaluronic acid, collagen and elastin in the mechanical properties of connective tissues. *J Anat*. 1980;131(Pt 4):611-620. http://www.ncbi.nlm.nih.gov/pubmed/7216901%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC1233214
16. Papakonstantinou E, Roth M, Karakiulakis G. Hyaluronic acid: A key molecule in skin aging. *Dermatoendocrinol*. 2012;4(3):253-258. doi:10.4161/derm.21923
17. Robert L, Robert AM, Renard G. Effets biologiques de l’hyaluronane dans les

tissus conjonctifs, l'œil, la peau, la paroi veineuse. Rôle dans le vieillissement. *Pathol Biol*. 2010;58(3):187-198. doi:10.1016/j.patbio.2009.09.010
18. Choi WY, Cho HW, Lee DW. Complications of Injectable Soft Tissue Filler. *Arch Aesthetic Plast Surg*. 2015;21(1):1. doi:10.14730/aaps.2015.21.1.1
19. Urdiales-Gálvez F, Delgado NE, Figueiredo V, et al. Treatment of Soft Tissue Filler Complications: Expert Consensus Recommendations. *Aesthetic Plast Surg*. 2018;42(2):498-510. doi:10.1007/s00266-017-1063-0
20. Beleznay K, Carruthers JDA, Humphrey S, Jones D. Avoiding and treating blindness from fillers: A review of the world literature. *Dermatologic Surg*. 2015;41(10):1097-1117. doi:10.1097/DSS.0000000000000486
21. Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, Jones D. Update on Avoiding and Treating Blindness From Fillers: A Recent Review of the World Literature. *Aesthetic Surg J*. Published online February 2019. doi:10.1093/asj/sjz053
22. Koziej M, Polak J, Hołda J, et al. The Arteries of the Central Forehead: Implications for Facial Plastic Surgery. *Aesthetic Surg J*. 2020;40(10):1043-1050. doi:10.1093/asj/sjz295
23. Schünke M, Schulte E, Schumacher U, Voll M, Wesker KH. 5.17 Einteilung und Leitungsbahnen der Augenhöhle (Orbita). In: Schünke M, Schulte E, Schumacher U, Voll M, Wesker KH, eds. 5. Auflage. Georg Thieme Verlag; 2018. doi:10.1055/b-006-149644
24. Loh KTD, Chua JJ, Lee HM, et al. Prevention and management of vision loss relating to facial filler injections. *Singapore Med J*. 2016;57(8):438-443. doi:10.11622/smedj.2016134
25. Zein M, Tie-Shue R, Pirakitikulr N, Lee WW. Complications after cosmetic periocular filler: prevention and management. *Plast Aesthetic Res*. 2020;2020. doi:10.20517/2347-9264.2020.133
26. Cho K-HH, Dalla Pozza E, Toth G, Bassiri Gharb B, Zins JE. Pathophysiology Study of Filler-Induced Blindness. *Aesthetic Surg J*. 2019;39(1):96-106. doi:10.1093/asj/sjy141
27. Chatrath V, Banerjee PS, Goodman GJ, Rahman E. Soft-tissue Filler-associated Blindness: A Systematic Review of Case Reports and Case Series. *Plast Reconstr surgery Glob open*. 2019;7(4):e2173. doi:10.1097/GOX.0000000000002173
28. Hirsch P, Infanger M, Kraus A. A case of upper lip necrosis after cosmetic injection of hyaluronic acid soft-tissue filler—Does capillary infarction play a role in the development of vascular compromise, and what are the implications? *J Cosmet Dermatol*. 2020;19(6):1316-1320. doi:10.1111/jocd.13391
29. Beleznay K, Humphery S, Carruthers JDA, Carruthers A. Vascular Compromise from Soft Tissue Augmentation. *J Clin Aesthet Dermatol*. 2014;7(9):37-43. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4174919/
30. Daly L, Ridgway J, Nelson J, Lowe N, Wong B. Calcium hydroxylapatite associated soft tissue necrosis: A case report and treatment guideline. *J Plast Reconstr Aesthet Surg*. 2013;67. doi:10.1016/j.bjps.2013.08.008
31. Moore RM, Mueller MA, Hu AC, Evans GRD. Asymptomatic Stroke After Hyaluronic Acid Filler Injection: Case Report and Literature Review. *Aesthetic Surg J*. Published online December 2020. doi:10.1093/asj/sjaa381
32. Lee S, Jung J, Seo J, Kim E-G. Ischemic Stroke Caused by a Hyaluronic Acid Gel Embolism Treated with Tissue Plasminogen Activator. *J Neurocritical Care*. 2017;10(2):132-135. doi:10.18700/jnc.170020
33. Köhler LD, Schwedler S, Worret WI. Embolia cutis medicamentosa. *Int J*

Dermatol. 1997;36(3):197. doi:10.1046/j.1365-4362.1997.00233.x
34. Marangi GF, Gigliofiorito P, Toto V, Langella M, Pallara T, Persichetti P. Three cases of embolia cutis medicamentosa (Nicolau's syndrome). *J Dermatol*. 2010;37(5):488-492. doi:10.1111/j.1346-8138.2010.00864.x
35. Cotofana S, Lachman N. Arteries of the Face and Their Relevance for Minimally Invasive Facial Procedures: An Anatomical Review. *Plast Reconstr Surg*. 2019;143(2):416-426. doi:10.1097/PRS.0000000000005201
36. Meegalla N, Sood G, Nessel TA, Downs BW. Anatomy, Head and Neck, Facial Arteries. In: ; 2022.
37. Hong SJ, Park SE, Jo JW, et al. Variant facial artery anatomy revisited: Conventional angiography performed in 284 cases. *Medicine (Baltimore)*. 2020;99(28):e21048. doi:10.1097/MD.0000000000021048
38. Kumar N, Rahman E. Effectiveness of teaching facial anatomy through cadaver dissection on aesthetic physicians' knowledge. *Adv Med Educ Pract*. 2017;8:475-480. doi:10.2147/AMEP.S139893
39. Kumar N, Swift A, Rahman E. Development of "Core Syllabus" for Facial Anatomy Teaching to Aesthetic Physicians: A Delphi Consensus. *Plast Reconstr surgery Glob open*. 2018;6(3):e1687. doi:10.1097/GOX.0000000000001687
40. Vural E, Batay F, Key JM. Glabellar frown lines as a reliable landmark for the supratrochlear artery. *Otolaryngol - Head Neck Surg*. 2000;123(5):543-546. doi:10.1067/mhn.2000.110540
41. Ugur MB, Savranlar A, Uzun L, Küçüker H, Cinar F. A reliable surface landmark for localizing supratrochlear artery: Medial canthus. *Otolaryngol - Head Neck Surg*. 2008;138(2):162-165. doi:10.1016/j.otohns.2007.11.005
42. Park HJ, Lee J-H, Lee K-L, Choi Y-J, Hu K-S, Kim H-J. Ultrasonography Analysis of Vessels Around the Forehead Midline. *Aesthetic Surg J*. Published online December 2020. doi:10.1093/asj/sjaa354
43. Choi DY, Bae JH, Youn KH, et al. Topography of the dorsal nasal artery and its clinical implications for augmentation of the dorsum of the nose. *J Cosmet Dermatol*. 2018;17(4):637-642. doi:10.1111/jocd.12720
44. Cotofana S, Pretterklieber B, Lucius R, et al. Distribution pattern of the superior and inferior labial arteries: Impact for safe upper and lower lip augmentation procedures. *Plast Reconstr Surg*. 2017;139(5). doi:10.1097/PRS.0000000000003244
45. Lee S-H, Gil Y-C, Choi Y-J, Tansatit T, Kim H-J, Hu K-S. Topographic Anatomy of the Superior Labial Artery for Dermal Filler Injection. *Plast Reconstr Surg*. 2015;135(2):445-450. doi:10.1097/PRS.0000000000000858
46. Money SM, Wall WB, Davis LS, Edmondson AC. Lumen Diameter and Associated Anatomy of the Superior Labial Artery With a Clinical Application to Dermal Filler Injection. *Dermatologic Surg*. Published online August 2019:1. doi:10.1097/dss.0000000000002074
47. Cong LY, Phothong W, Lee SH, et al. Topographic Analysis of the Supratrochlear Artery and the Supraorbital Artery: Implication for Improving the Safety of Forehead Augmentation. *Plast Reconstr Surg*. 2017;139(3):620e--627e. doi:10.1097/PRS.0000000000003060
48. Kleintjes WG. Forehead anatomy: arterial variations and venous link of the midline forehead flap. *J Plast Reconstr Aesthet Surg*. 2007;60(6):593-606. doi:10.1016/j.bjps.2006.12.006
49. Loukas M, Hullett J, Louis RG, et al. A detailed observation of variations of the facial artery, with emphasis on the superior labial artery. *Surg Radiol Anat*. 2006;28(3):316-324. doi:10.1007/s00276-006-0093-0

50. Wegrzyn M, Vogt M, Kireclioglu B, Schneider J, Kissler J. Mapping the emotional face. How individual face parts contribute to successful emotion recognition. *PLoS One*. 2017;12(5):1-15. doi:10.1371/journal.pone.0177239
51. Zhou B, Ghose T, Lukowicz P. Expressure: Detect Expressions Related to Emotional and Cognitive Activities Using Forehead Textile Pressure Mechanomyography. *Sensors (Basel)*. 2020;20(3). doi:10.3390/s20030730
52. Guarnera M, Hichy Z, Cascio MI, Carrubba S. Facial Expressions and Ability to Recognize Emotions From Eyes or Mouth in Children. *Eur J Psychol*. 2015;11(2):183-196. doi:10.5964/ejop.v11i2.890
53. Lee KL, Lee HJ, Youn KH, Kim HJ. Positional relationship of superior and inferior labial artery by ultrasonography image analysis for safe lip augmentation procedures. *Clin Anat*. Published online 2019. doi:10.1002/ca.23379
54. Tansatit T, Apinuntrum P, Phetudom T. A typical pattern of the labial arteries with implication for lip augmentation with injectable fillers. *Aesthetic Plast Surg*. 2014;38(6):1083-1089. doi:10.1007/s00266-014-0401-8
55. Correa BJ, Weathers WM, Wolfswinkel EM, Thornton JF. The forehead flap: the gold standard of nasal soft tissue reconstruction. *Semin Plast Surg*. 2013;27(2):96-103. doi:10.1055/s-0033-1351231
56. Smart RJ, Yeoh MS, Kim DD. Paramedian forehead flap. *Oral Maxillofac Surg Clin North Am*. 2014;26(3):401-410. doi:10.1016/j.coms.2014.05.008
57. Hammer D, Williams F, Kim R. Paramedian Forehead Flap. *Atlas Oral Maxillofac Surg Clin North Am*. 2020;28(1):23-28. doi:10.1016/j.cxom.2019.11.003
58. Ahmadi SK, Rahpeyma A, Rezvani HN. Vermilion lower lip cross flap - An anatomic study on 22 fresh cadavers. *Ann Maxillofac Surg*. 2012;2(2):107-110. doi:10.4103/2231-0746.101327

Danksagung

In tiefster Dankbarkeit widme ich diese Dissertation den Menschen, die mich stets bei der Erreichung meiner Ziele unterstützt haben.

Hierbei möchte ich insbesondere meine Eltern sowie Prof. Dr. med. Thilo Schenck, Prof. Dr. Sebastian Cotofana und Dr. med. Dr. med. univ. Konstantin Frank danken. Ohne die Unterstützung wäre es mir nicht möglich gewesen, diese Dissertation anzufertigen.

Vielen Dank für alles.