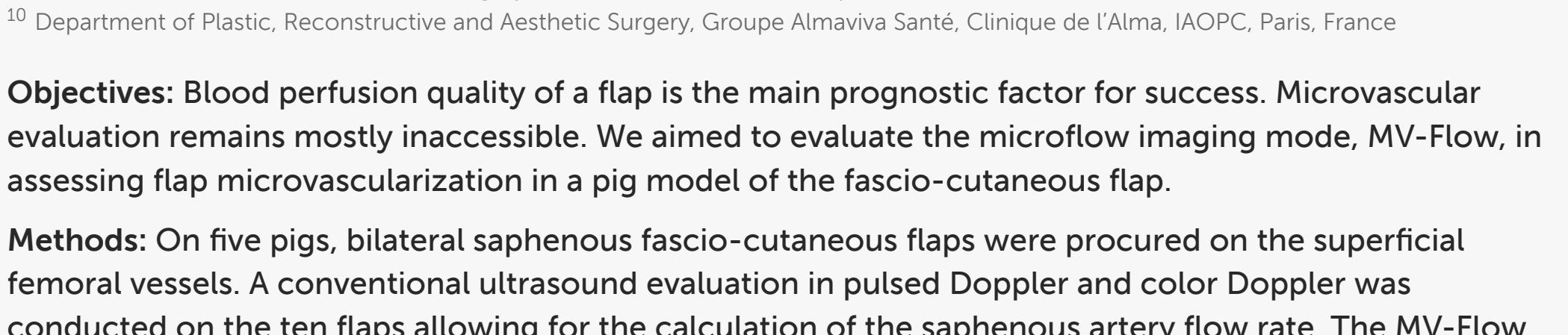


ORIGINAL RESEARCH article

Front. Physiol. 15 December 2022
Sec. Medical Physics and Imaging
Volume 13 – 2022 | <https://doi.org/10.3389/fphys.2022.1063240>

Microvascular assessment of fascio-cutaneous flaps by ultrasound: A large animal study



¹ Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
² Hôpital Européen Georges-Pompidou, Assistance Publique—Hôpitaux de Paris (APHP), Université Paris-Cité, Paris, France
³ Shriners Children's Boston, Boston, MA, United States
⁴ Centre Hospitalier Universitaire de Rennes, Université de Rennes 1, Rennes, France
⁵ Division of Plastic and Reconstructive Surgery, Vascularized Composite Allotransplantation Laboratory Center for Transplantation Sciences, Massachusetts General Hospital Harvard Medical School, Boston, MA, United States
⁶ Center for Engineering in Medicine and Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
⁷ Division of Cardiac Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
⁸ University Clinic of Cardiac Surgery, Leipzig Heart Center, Leipzig, Germany
⁹ Division of Vascular and Endovascular Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
¹⁰ Department of Plastic, Reconstructive and Aesthetic Surgery, Groupe Airmaiva Santé, Clinique de l'Alma, IAOFC, Paris, France

Objectives: Blood perfusion quality of a flap is the main prognostic factor for success. Microvascular evaluation remains mostly inaccessible. We aimed to evaluate the microflow imaging mode, MV-Flow, in increasing flap microvascularization in a pig model of the fascio-cutaneous flap.

Methods: On five pigs, bilateral saphenous fascio-cutaneous flaps were procured on the superficial femoral vessels. A conventional ultrasound evaluation in pulsed Doppler and color Doppler was conducted on the ten flaps allowing for the calculation of the saphenous artery flow rate. The MV-Flow mode was then applied: for qualitative analysis, with identification of saphenous artery collaterals; then quantitative, with repeated measurements of the Vascularity Index (VI), percentage of pixels where flow is detected relative to the total ultrasound view area. The measurements were then repeated after increasing arterial flow by clamping the distal femoral artery.

Results: The MV-Flow mode allowed a better follow-up of the saphenous artery's collaterals and detected microflows not seen with the color Doppler. The VI was correlated to the saphenous artery flow rate (Spearman rho of 0.64; $p = 0.002$) and allowed to monitor the flap perfusion variations.

Conclusion: Ultrasound imaging of microvascularization by MV-Flow mode and its quantification by VI provides valuable information in evaluating the microvascularization of flaps.

1 Introduction

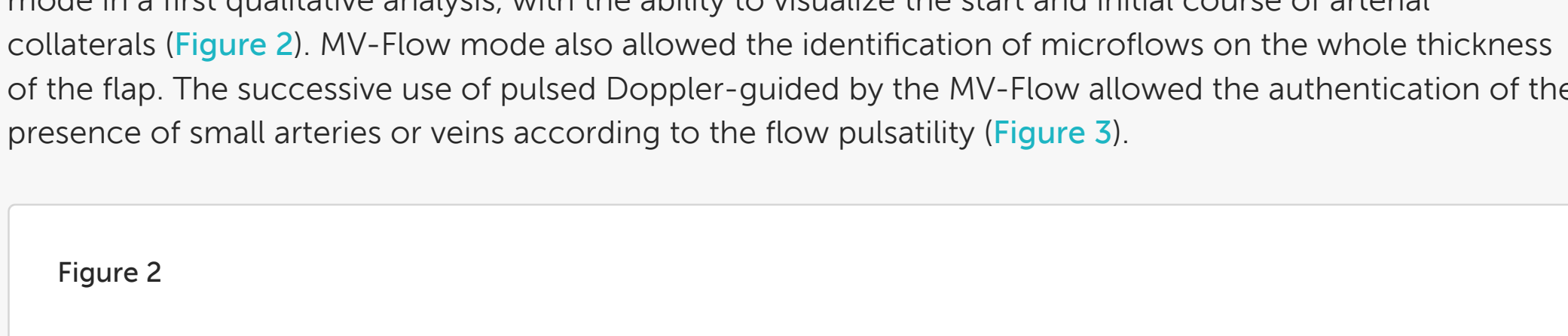
Fascio-cutaneous flaps have become the gold-standard technique for complex defect reconstruction (Paro et al., 2016). By sparing the muscle while providing a vascularized skin paddle, the surgeon can cover defects near or distant from the donor site by performing pedicled or free fascio-cutaneous flaps (Cariou, 1995; Boretto and De Cicco, 2022). Assessment of segmental perfusion of a fascio-cutaneous flap is an important viability factor, although challenging in daily practice. When perfusion failure is suspected during surgery and postoperatively, a prompt assessment is mandatory to consider arterial or venous thrombosis and to allow a possible therapeutic procedure (Liu et al., 2020). Ultrasound imaging is particularly suitable because of its ease of use and ability to evaluate superficial tissue with good image quality. However, conventional Doppler modes only allow a limited assessment of flap perfusion, and most microvascularization remains inaccessible. Nevertheless, access to an evaluation of the microvascular network is a major challenge because the good capacity of the underlying microvascular network is responsible for the good perfusion of the flap. New ultrasonic methods dedicated to slow flow visualization have been recently developed to access the microvascular network, such as MV-Flow (Gettle and Revzin, 2020; Giuffrida et al., 2021). Based on a high frame rate associated with dedicated filters, MV-Flow allows a high sensitivity of flow measurements in small arterioles and venules, giving access to a vascular mapping of tissue (Aghabaglou et al., 2022).

Our objective was to evaluate the MV-Flow mode's ability to assess flap microvascularization in a clinically relevant large animal model by evaluating its potential to detect arteriolar and venular microflows and quantify perfusion changes.

2 Methods

2.1 Experimental flap model

All animal care and use in the present study were approved by the Massachusetts General Hospital (Boston, MA, United States) Institutional Animal Care and Use Committee (Protocol 2020N00015). Ten saphenous fascio-cutaneous flaps were procured from five 30–35 kg Yorkshire pigs under general anesthesia. As previously described by Pozzo et al. (Pozzo et al., 2022), the distal saphenous pedicle was ligated to allow the flap to be elevated distally to proximally (Figure 1). The vessel dissection was performed up to the femoral vessels, which were subsequently dissected (Supplementary Video S1). After flap elevation, a single dose of heparin (100 UI/kg) was given intravenously before the ultrasound evaluation. The ultrasonic assessment was performed at the end of the bilateral flap harvesting. After initial ultrasound analysis, the femoral artery was clamped distally to the saphenous pedicle (Figure 1) to increase flap perfusion.



2.2 Ultrasound Imaging

Ultrasound examination was performed with a Samsung RS85[®] (Samsung Medison Co., Seoul, Korea). We performed flap views with minimal compression to obtain the best microvascularization analysis using MV-Flow mode (Supplementary Video S2). The Vascularity Index (VI) corresponds to the percentage of pixels where flow is detected relative to the total ultrasound evaluation area (Chen et al., 2021; Baek et al., 2022). Three measurements of VI were performed in a standardized format during systole in a 2.0 cm² region of interest, starting at the level of the superficial dermis and excluding the saphenous artery. Three measurements of VI were performed in a standardized format: measurement in systole (for small arteries, this allowed to obtain a better flow) from video back-up.

The baseline arterial flow rate was measured on the proximal saphenous artery and obtained by the average of three measures with an automated record of the mean velocity by pulsed Doppler, and measurement of the internal diameter of the artery by color Doppler, by the average of two diastolic and one systolic measurement. The flow rate in the femoral artery was also measured similarly, by three pulsed Doppler mean velocity measurements and three transverse artery diameter measurements. Intra-observer repeatability of VI measurements was calculated based on 10 VI measurements by a single observer. Sequential measurements of two observers on different ultrasonic acquisitions assessed inter-observer variations.

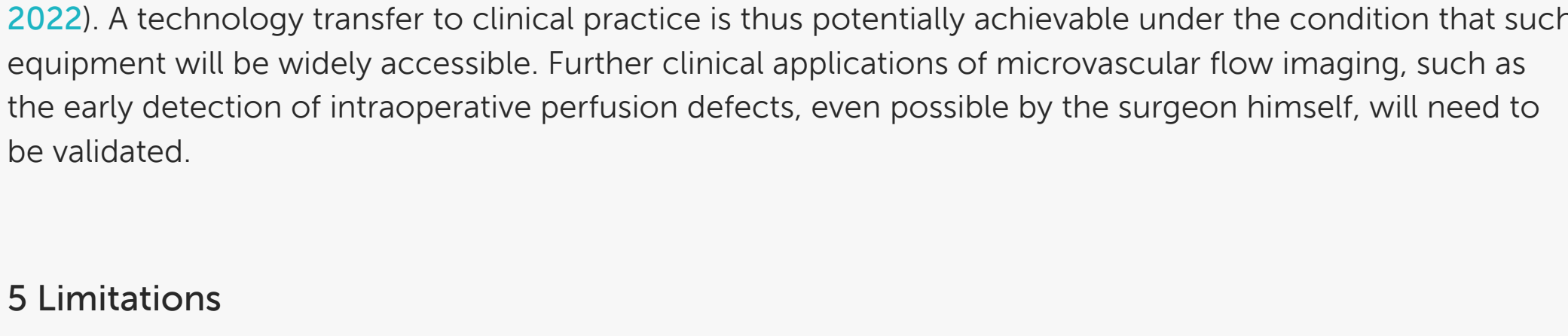
2.3 Statistical analysis

Continuous variables are presented by the median [25th–75th percentiles]. A Wilcoxon signed-rank test was used for paired data comparisons. The correlation was performed using a Spearman rank test. The interclass correlation coefficient (ICC) assessed the reliability of VI. Statistical significance was considered at the 0.05 level. Analyses were performed using R[®] software (R-Studio, Boston, MA, United States).

3 Results

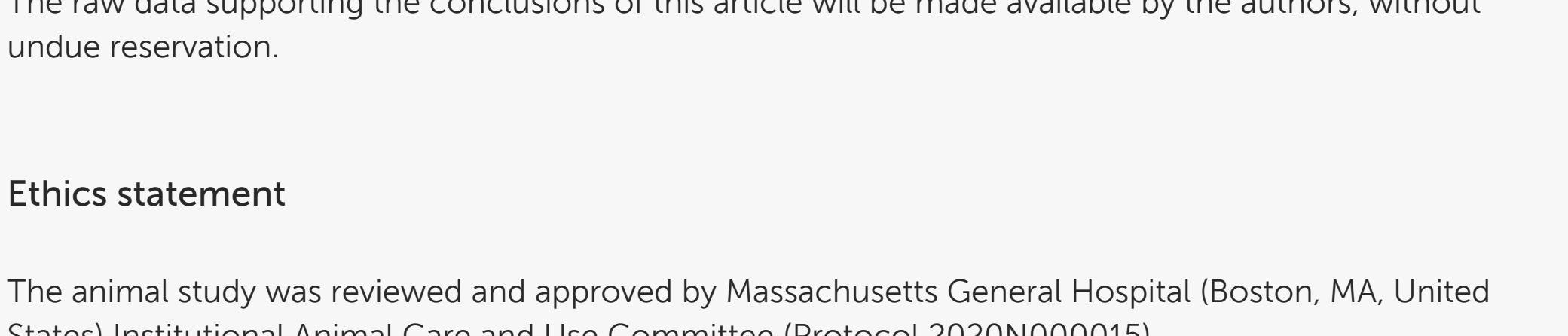
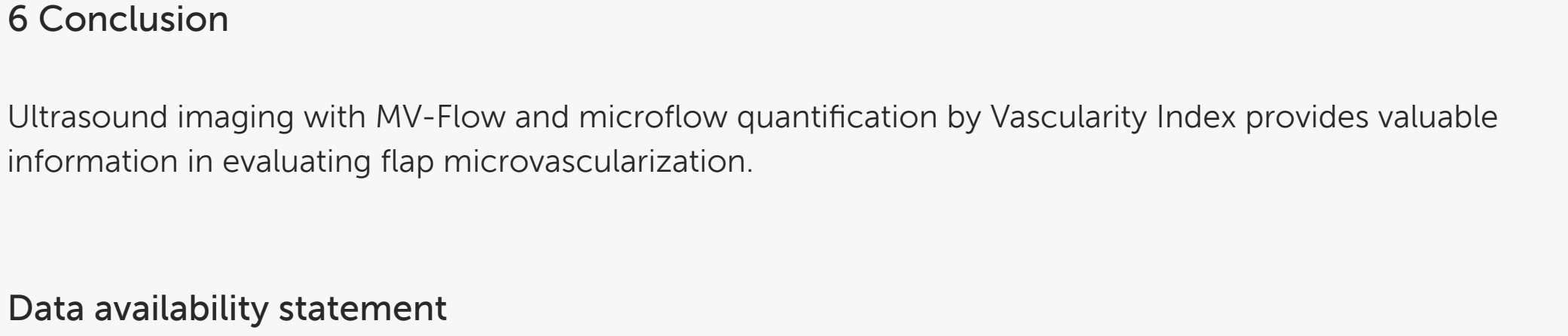
3.1 Conventional ultrasonic assessment of arterial flow in the flap

Good vascular patency was noted for all ten flaps. The mean velocity over the cardiac cycle of the saphenous artery was 1.31 cm/beat [0.84–2.43] with a flow rate of 1.13 mL/min [0.87–1.37] (Table 1). This corresponded to an average of 2.3% of the femoral artery flow rate measured at 79.7 mL/min [53.5–118.4].



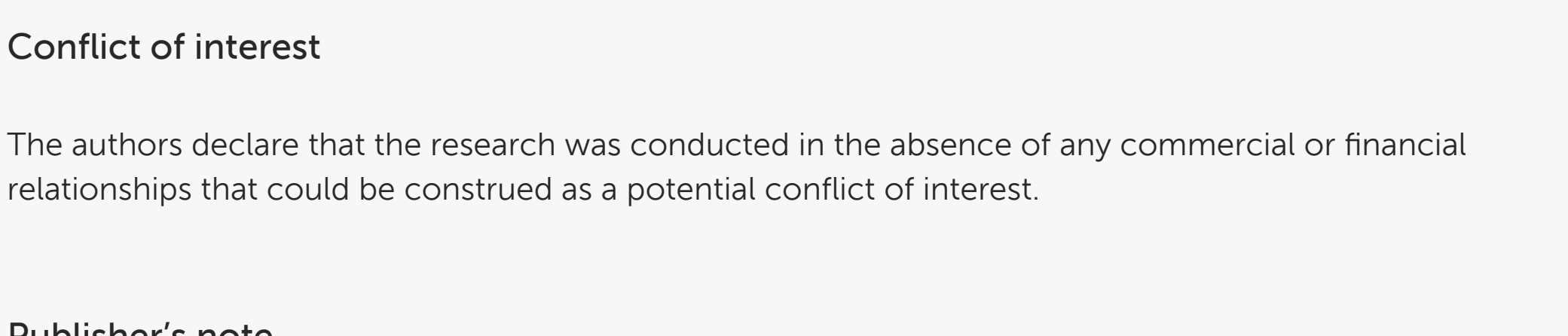
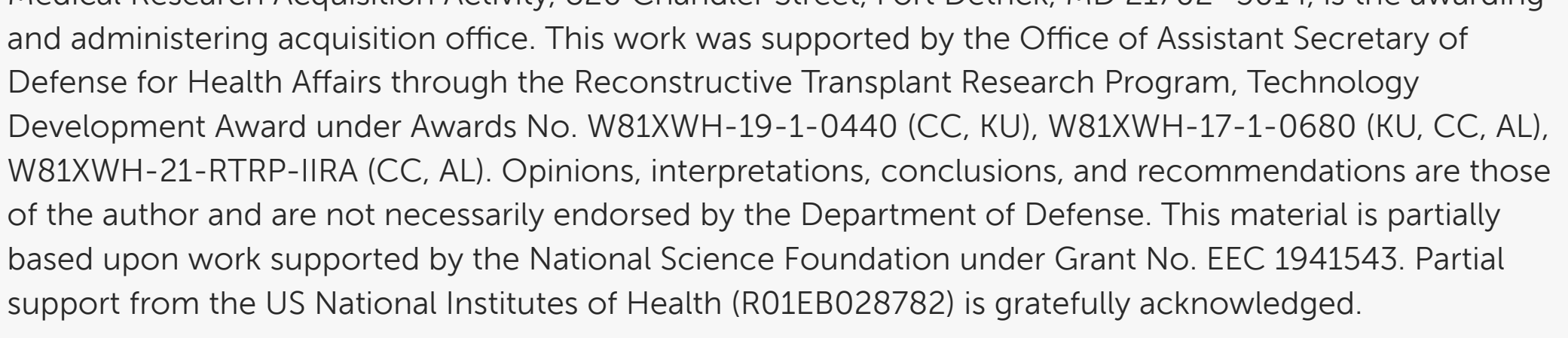
3.2 Qualitative evaluation of the MV-Flow mode: identification of microvessels

MV-Flow mode allowed better visualization of the saphenous artery trajectory than the color Doppler mode in a first qualitative analysis, with the ability to visualize the start and initial course of arterial collaterals (Figure 2). MV-Flow mode also allowed the identification of microflows on the whole thickness of the flap. The successive use of pulsed Doppler-guided by the MV-Flow allowed the authentication of the presence of small arteries or veins according to the flow pulsatility (Figure 3).



3.3 Quantitative evaluation by vascularity index: Detection of local perfusion changes

The distal femoral artery clamping maneuver was associated with improved visual pulsatility of the saphenous artery and a notable increase in diameter. The flow rate increase was noted by ultrasound: 1.98 mL/min [1.58–2.70] vs 1.13 [0.87–1.37], $p = 0.004$ (Table 1). Outside the field of view of the artery, the VI was significantly increased: 6.93 [4.82–8.67] vs 3.15 [2.48–4.38], $p = 0.002$ (Table 1; Figures 4, 5). There was a good correlation between saphenous arterial flow and VI (Spearman rho of 0.64; $p = 0.002$).



3.4 Intra- and inter-observer reliability of Vascularity Index

Intra-observer and inter-observer ICC were respectively 0.86 and 0.95 for the VI, thus showing a good reproducibility of the measurements.

4 Discussion

In this work, MV-flow mode allowed the visualization of small superficial vessels and the micro vascularization quantification related to the flap perfusion, not accessible with conventional Doppler. Currently expanding, the use of methods dedicated to micro vascularization is still limited, with little validation and low accessibility of new-generation devices until now. Nevertheless, they allow for easy characterization of microflows, opening up many clinical applications (Jin et al., 2022; Tang et al., 2022).

The Vascularity Index seems particularly useful as it provides a simple and segmental quantification of vascularization. Applied to the fascio-cutaneous flap, it brings an easier detection of small arteries and veins, with a potential impact during intraoperative use (Tashiro et al., 2016). Furthermore, it allows a local estimation of the perfusion, which can be segmental, and does not require the registration of the feeding artery, which is sometimes not easily accessible in case of a deep artery or poor image quality. Lastly, this mode does not require a dedicated recording device as microvascular flow imaging modes are now included in many ultrasound scanners of most of the companies (Gettle and Revzin, 2020; Aziz et al., 2022). A technology transfer to clinical practice is thus potentially achievable under the condition that such equipment will be widely accessible. Further clinical applications of microvascular flow imaging, such as the early detection of intraoperative perfusion defects, even possible by the surgeon himself, will need to be validated.

5 Limitations

The VI has only been used to quantify highly vascularized organs such as the thyroid (mean values of normal thyroid around 20%) or placenta (mean values of normal placenta around 45%) (Chen et al., 2021; Baek et al., 2022). We present the first evaluation on the skin, much less vascularized, thus facing the challenge of accurate signal measurement without motion artifacts. Since *in vivo* microvascular assessment technologies are limited, this study lacks comparison to a gold standard Imaging method. While no reference values are available to compare our data, we expect that our values will be used as a comparison for future studies. Doppler quantification of the arterial flow rate was performed to overcome this limitation by giving insight into global flap perfusion. Another limitation is that the VI has not been directly compared to visualization in color Doppler. A color Doppler vascularity index has been proposed for organs that are more perfused than the fascio-cutaneous flap, such as the kidney or the thyroid (Chen et al., 2002; Sultan et al., 2015; Zhang et al., 2022). In these cases, the higher blood flow velocities allowed for color mapping and area comparison with conventional Doppler. However, this was not the case for cutaneous and subcutaneous tissues where low blood flow velocities resulted in poor color Doppler visualization. Lastly, VI should be ideally measured in 3D. A perspective is the use of a 3D mode of microvascular imaging currently arising (Zhang et al., 2019; Cai et al., 2021).

6 Conclusion

Ultrasound imaging with MV-Flow and microflow quantification by Vascularity Index provides valuable information in evaluating flap microvascularization.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The animal study was reviewed and approved by Massachusetts General Hospital (Boston, MA, United States) Institutional Animal Care and Use Committee (Protocol 2020N00015).

Author contributions

AL, BU, and CG conceived the study. AL and BU supervised the study. GG and YB collected the data. YB, EC-T, and GG performed the surgery. GG and YB performed the statistical analysis. GG and YB wrote the manuscript. All authors interpreted the data, drafted, and revised the manuscript, and approved the final version.

Funding

GG was funded by the Federation Française de Cardiologie and the Institut Servier. YB was funded by CHU de Rennes, Fondation des Gueules Cassées and Shriners Children Boston (#84308-BOS-22). Shriners Hospitals partially funded this work for Children grant #85127-BOS-20 (BU) and 85015-BOS-23 (KU, CC, AL). AK was funded by the American Heart Association Postdoctoral Fellowship Award. The US Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick, MD 21702–5014, is the awarding and administering acquisition office. This work was supported by the Office of Assistant Secretary of Defense for Health Affairs through the Reconstructive Transplant Research Program, Technology Development Award under Awards No. W81XWH-19-1-0440 (CC, KU), W81XWH-17-1-0680 (KU, CC, AL), W81XWH-21-RTRP-IIRA (CC, AL). Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the Department of Defense. This material is partially based upon work supported by the National Science Foundation under Grant No. EEC 1941543. Partial support from the US National Institutes of Health (R01EB028782) is gratefully acknowledged.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fphys.2022.1063240/full#supplementary-material>

References

Aghabaglou F, Ainechi A, Abramson H, Curry E, Kaovasia T, P, Kamal S, (2022). Ultrasound monitoring of microcirculation: An original study from the laboratory bench to the clinic. *Microcirculation* 29, e12770. doi:10.1111/micc.12770

PubMed Abstract | CrossRef Full Text | Google Scholar

Aziz M, U, Eisenbrey J, Deganello A, Zahid M, Sharbidre K, Sidhu P, (2022). Microvascular flow imaging: A state-of-the-art review of clinical use and promise. *Radiology* 305, 250–264. doi:10.1148/radiol.213303

PubMed Abstract | CrossRef Full Text | Google Scholar

Baek H-S, Park J-Y, Jeong C-H, Ha J, Kang M, I, L, Lim D-J, (2022). Usefulness of real-time quantitative microvascular ultrasonography for differentiation of graves' disease from destructive thyroiditis in thyrotoxic patients. *Endocrinol. Metab* 37, 323–332. doi:10.3803/enm.2022.1413

PubMed Abstract | CrossRef Full Text | Google Scholar

Boretto J, G, De Cicco F, L (2022). *Fasciocutaneous flaps*. StatPearls Publishing.

Google Scholar

Cai S, Wang H, Zhang X, Zhang L, Zhu Q, Sun Q, (2021). Superb microvascular imaging technology can improve the diagnostic efficiency of the BI-rads system. *Front. Oncol* 11, 634752. doi:10.3389/fonc.2021.634752

PubMed Abstract | CrossRef Full Text | Google Scholar

Cariou J, L (1984–1994). *Ten Years Of Skin Flaps: Progress And Conceptual Changes Or Changes In Vascular Classification, And Clinical Concepts*. Annales de Chirurgie Plastique Esthétique, 447–525.

Google Scholar

Chen C, N, Cheng Y, M, Lin M, T, Hsieh F, J, Lee P, H, Chang K, J (2002). Association of color Doppler vascularity index and microvessel density with survival in patients with gastric cancer. *Ann. Surg* 235, 512–518. doi:10.1097/00000658-200204000-00009

PubMed Abstract | CrossRef Full Text | Google Scholar

Chen X, X, Wei X, Zhao S, Huang H, Wang W, Qiu J, (2021). Characterization of placental microvascular architecture by MV-flow imaging in normal and fetal growth-restricted pregnancies. *J. Ultrasound Med* 40, 1533–1542. doi:10.1002/jum.15531

PubMed Abstract | CrossRef Full Text | Google Scholar

Gettle L, M, Revzin M, V (2020). Innovations in vascular ultrasound. *Radiol. Clin. North Am* 58, 653–669. doi:10.1016/j.rcl.2020.03.002

PubMed Abstract | CrossRef Full Text | Google Scholar

Giuffrida A, B, Araujo Junior E, (2021). My-flow and lumiflow: New Doppler tools for evaluating the microvascularization of the fetal head. *Radiol. Bras* 54, 348–349. doi:10.1590/0100-3984.2020.0137

PubMed Abstract | CrossRef Full Text | Google Scholar

Jin H, Wang C, Jin X, (2022). Superb microvascular imaging for distinguishing thyroid nodules: A meta-analysis (prisma). *Med. Baltim* 101, e29505. doi:10.1097/MD.00000000000029505

PubMed Abstract | CrossRef Full Text | Google Scholar

Liu C, Li P, Liu J, Xu Y, Wu H, Gong Z, (2020). Management of intraoperative failure of anterolateral thigh flap transplantation in head and neck reconstruction. *J. Oral Maxillofac. Surg.* 78, 1027–1033. doi:10.1016/j.joms.2020.02.010

PubMed Abstract | CrossRef Full Text | Google Scholar

Paro J, Chiou G, Sen S, K (2016). Comparing muscle and fasciocutaneous free flaps in lower extremity reconstruction—does it matter? *Ann. Plast. Surg* 76, S213–S215. doi:10.1097/SAP.0000000000000779

PubMed Abstract | CrossRef Full Text | Google Scholar

Pozzo V, Romano G, Goutard M, Lupon E, Tawa P, Acun A, (2022). A reliable porcine fascio-cutaneous flap model for vascularized composite allografts bioengineering studies. *J. Vis. Exp.* 2022. doi:10.3791/63557

PubMed Abstract | CrossRef Full Text | Google Scholar

Sultan L, R, Xiong H, Zafar H, M, Schultz S, M, Langer J, E, Sehgal C, M (2015). Vascularity assessment of thyroid nodules by quantitative color Doppler ultrasound. *Ultrasound Med. Biol.* 41, 1287–1293. doi:10.1016/j.ultrasmedbio.2015.01.001

PubMed Abstract | CrossRef Full Text | Google Scholar

Tang K, Liu M, Zhu Y, Zhang M, Niu C, (2022). The clinical application of ultrasonography with superb microvascular imaging—a review. *J. Clin. Ultrasound* 50, 721–732. doi:10.1002/jcu.23210

PubMed Abstract | CrossRef Full Text | Google Scholar

Tashiro K, Yamashita S, Araki J, Narushima M, Iida T, Koshima I, (2016). Preoperative color Doppler ultrasonographic examination in the planning of thoracodorsal artery perforator flap with capillary perforators. *J. Plast. Reconstr. Aesthet. Surg* 69, 346–350. doi:10.1016/j.jbps.2015.10.026

PubMed Abstract | CrossRef Full Text | Google Scholar

Zhang L, Xu K, Ma L, Shao C, Gong C, Yu N, (2022). Nomogram model for predicting early onset of chronic kidney disease using color Doppler region of interest technique. *Abdom. Radiol. (New York)* 47, 4186–4194. doi:10.1007/s00261-022-03664-5

PubMed Abstract | CrossRef Full Text | Google Scholar

Zhang X, Y, Zhang L, Li N, Zhu Q, L, Li J, C, Sun Q, (2019). Vascular index measured by smart 3-D superb microvascular imaging can help to differentiate malignant and benign breast lesion. *Cancer Manag. Res* 11, S481–S487. doi:10.2147/CMAR.S203376

PubMed Abstract | CrossRef Full Text | Google Scholar

Keywords: vascularity index, microvascularization, flap surgery, pig, microcirculation, Microvascular flow imaging, MV-Flow

Citation: Goudot G, Berkane Y, de Clermont-Tonnerre E, Guinier C, Filz von Reiterdank I, van Kampen A, Uygun K, Cetrulo CL, Uygun BE, Dua A and Lelouch AG (2022) Microvascular assessment of fascio-cutaneous flaps by ultrasound: A large animal study. *Front. Physiol.* 13:1063240. doi:10.3389/fphys.2022.1063240

Received: 06 October 2022. **Accepted:** 28 November 2022.

Published: 15 December 2022.

Edited by: Xun Jia, Johns Hopkins Medicine, United States

Reviewed by: Ahmed El-Hazmy, Cairo University, Egypt

Francesco Falta, Institute of Clinical Physiology, Italy

Copyright: © 2022 Goudot, Berkane, de Clermont-Tonnerre, Guinier, Filz von Reiterdank, van Kampen, Uygun, Cetrulo, Uygun, Dua and Lelouch. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

*Correspondence: Guillaume Goudot, ggoudot@mgh.harvard.edu

Disclaimer: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claimed that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

People also looked at

Innovative Multiparametric Characterization of Carotid Plaque Vulnerability by Ultrasound

Guillaume Goudot, Lina Khider, Olivier Pedreira, Jonathan Poree, Pierre Julia, Jean-Marc Altsch, Kisaki Amemiya, Patrick Bruneau, Emmanuel Messas, Mathieu Pernot and Tristan Mirault

Methods: Aortic wall deformation assessment by ultrafast ultrasound imaging: Application to bicuspid aortic valve associated aortopathy

Guillaume Goudot, Charles Cheng, Alexis F. Guédon, Tristan Mirault, Olivier Pedreira, Alexandre Dahan, Louise Z. Wang, Mathieu Pernot and Emmanuel Messas

Building a successful minimally invasive mitral valve repair program before introducing the robotic approach: The Massachusetts General Hospital experience

Antonia van Kampen, Guillaume Goudot, Sophie Butte, Dane C. Paneitz, Michael A. Borger, Vinay Badnwar, Thoralf M. Sundt, Nathaniel B. Langer and Serguei Melnitchouk

Candidate Gene Resequencing in a Large Bicuspid Aortic Valve-Associated Thoracic Aortic Aneurysm Cohort: SMAD6 as an Important Contributor

Elisabeth Gillis, Ajay A. Kumar, Ilse Luyckx, Christoph Preuss, Elyssa Cannaearts, Gerard van de Beek, Björn Wieschendorf, Maaike Klaerts, Nikhita Bolar, Geert Vandeweyer, Josephina Meester, Florian Wünnemann, Russell A. Gould, Rustam Zhurayev, Dmytro Zerbino, Salah A. Mohamed, Seema Mital, Luc Mertens, Hanna M. Björck, Anders Franco-Cereceda, Andrew S. McCallion, Lut Van Laer, Judith M. A. Verhagen, Ingrid M. B. H. van de Laar, Marja W. Wessels, Emmanuel Messas, Guillaume Goudot, Michaela Nemcikova, Alice Krebsova, Marlies Kempers, Simone Saleminik, Toon Duijnhouwer, Xavier Jeunenaitre, Juliette Albuissou, Per Eriksson, Gregor Andelfinger, Harry C. Dietz, Aline Verstraeten, Bart L. Loeys and Mibava Leducq Consortium

Computational clustering reveals differentiated coronary artery calcium progression at prevalent levels of pulse wave velocity by classifying high-risk patients

Maximo Rousseau-Portalis, Leandro Cymberknop, Ignacio Farro and Ricardo Armentano