INNODERM

687866 — H2020-ICT-2015

D6.4: FINAL DISSEMINATION REPORT

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PU	Public	x
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

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1. Introduction

This document contains the final report on managing dissemination of results in INNODERM.

Over the course of the project, 21 papers and over 100 presentations on INNODERM research were produced. Of particular note is a clinical paper in Nature Biomedical Engineering on psoriasis imaging. Both the quality and quantity of publications and presentations were very high underlining the scientific output of the project and interest by outside researchers, potential commercial customers and the general public. Most of the papers and presentations focused on applications for the new imaging method, however also the technology partners contributed with technical content.

The Dissemination report deals with results that were put into the public domain. All of the content is by definition public. It addresses what publishable results have been produced and the method and location of dissemination, as well as which consortium members were involved in the respective activities.

The following sections describe the dissemination measures, including any scientific publications relating to results and foreground IP. The content was made available in the public domain thus demonstrating the added-value and positive impact of the project on the European Community. This report includes a list of all dissemination activities (publications, conferences, workshops, web, press releases, flyers, etc.) in free text format.

2. Knowledge Management and Dissemination Objectives

Dissemination and exploitation (with the protection of the intellectual property of our Consortium) are essential elements of the INNODERM project and have been actively sustained and updated based on developments throughout the project. In the next sections, we detail the steps we have taken to protect the project IP and disseminate the results to the widest audiences possible.

2.1. Knowledge Management

Management of knowledge, of intellectual property, and of other innovation-related activities arising from the project is one of the key tasks for Project Management. A Consortium Agreement covering these issues (among others) was signed by all partners at the beginning of the INNODERM project.

Rules for disclosure of Confidential Information within the consortium are set out in the Consortium Agreement. The Consortium has also formally agreed that Confidential Information

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may be disclosed to 3rd parties outside the Consortium on a need-to-know basis under a Non-Disclosure Agreement (NDA) with format approved by the Consortium.

2.1. Dissemination Channels

During the project we have focused our dissemination activities on audiences including:

1. Clinicians and academic researchers in the fields of optoacoustic and medical imaging, medical devices, cardio-metabolic and skin inflammatory conditions
2. Healthcare and Investment Industry professionals
3. Health Insurance Industry professionals
4. Engineering Industry professionals
5. Policymakers

Various means of dissemination and a number of specific dissemination measures were outlined in the Grant Agreement including the creation and use of a logo, implementation of public and internal project websites, social media channels, publications in scientific journals, scientific conference and workshop contributions, and press releases and general media contributions. We outline these dissemination channels and the results of our dissemination efforts in the next sections. Detailed information about dissemination activities throughout the project can be found in previously submitted deliverables.

2.2.1. Public Website

A public website (http://innoderm2020.eu/) was created at the beginning of the project in 2016. The website details the project objectives and achievements, provides links and descriptions for each of the Consortium partners, and acts as an organ for dissemination of publicly available non-peer-reviewed information such as press releases and information sheets. This website is maintained by consortium member TUM.

Google Analytics tracking of the website was enabled beginning of 2019. Since then, and linked to the launch of our social media presence on Twitter in December 2018, the number of visitors has increased steadily. In the first years of the project, the majority of interest came from Germany and within the EU, however in 2021 there has been a significant increase in overseas interest including the United States, Japan and Russia (Figure 2.2.1.1.).

2.2.2. Scientific Publications

The main measurable output of the scientific partners in the consortium are scientific publications in peer-reviewed journals. The publication register in Table 1 gives an overview of INNODERM publications, the partners involved as well as the related work package.

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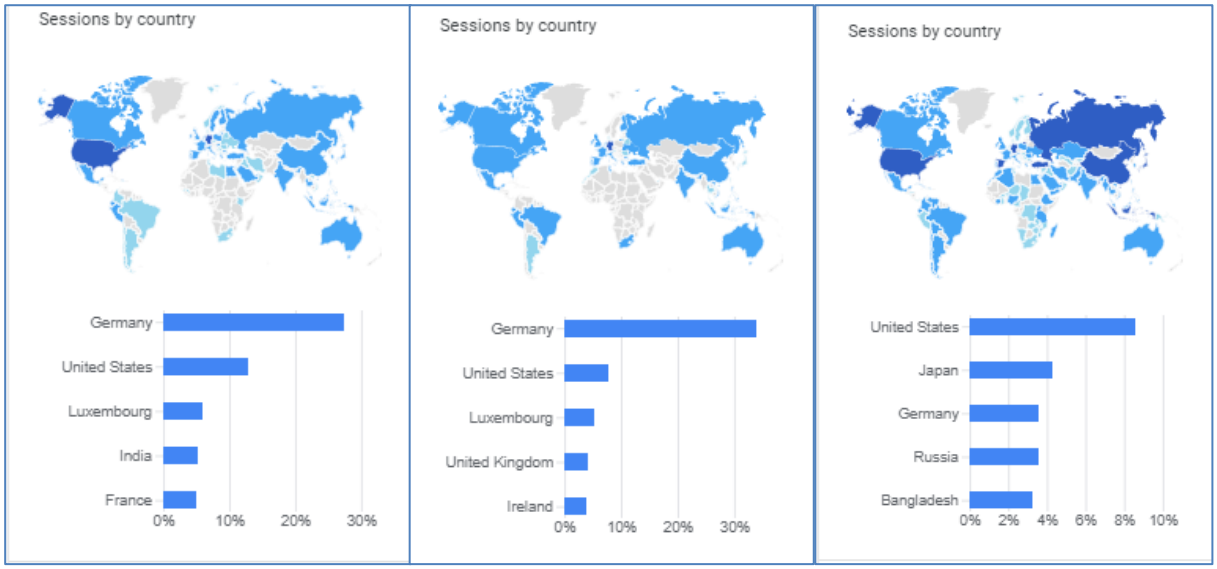

Figure 2.2.1.1. INNODERM website sessions by country during 2019 (left), 2020 (middle) and 2021

In addition to publications, the INNODERM partners also track performance of publications (if possible) by different metrics including the number of citations or the Altmetric score. For example, publication 3 from the register currently lists 135 citations and an Altmetric score of 119, which means it is better than 97% of tracked articles of a similar age in all journals and better than 81% of articles of a similar age in Nature Biomedical Engineering.

In addition, in 2018 one of the publications resulting from the INNODERM project won an award for top-downloaded article by the publisher Wiley (see Appendix 1).

2.2.3. Application Notes

From the scientific output provided by all partners, iThera created specific 2-page application notes to be distributed to interested parties and potential customers by mail, email or at exhibitions, talks and conferences. Overall, six different application notes were created on the topics of Clinical Skin Imaging, High-resolution RSOM Imaging, Inflammatory Skin Diseases, Preclinical IBD Imaging, Psoriasis Imaging, and Vasodilation Imaging. An example for an RSOM application note is attached as Appendix 2.

2.2.4. Targeted Mailings

iThera has and continues to approach potential customers for RSOM prototype systems in research institutes by targeted mails following in-depth analysis of their research topics and publications. Eight campaigns were run on RSOM-related content over the course of the INNODERM project. The results of these campaigns are shown in Table 2.2.4.1.

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Table 2.2.4.1. Results of RSOM mailing campaigns by iThera Medical to potential customers.

Date	Topic	Recipients
June 2017	Clinical Psoriasis (early test campaign)	20
March 2018	Preclinical gastro	187
April 2018	Clinical systemic sclerosis	98
March 2020	Imaging Tumor Function and Response with Optoacoustics	13,749
Oct 2020	A novel view on skin inflammation by means of RSOM	7,088
March 2021	Optoacoustic Imaging in Dermatology (H2020 Innoderm)	7,253
April 2021	RSOM for diabetes / microcirculation	731
April 2021	3D Imaging of Vascular Anomalies Using RSOM	7,882

Several of the above responses have moved to opportunity stage meaning that the customer is aware of the value of the technology for his research and is actively looking for funding for the purchase.

2.2.5. Social Media

The INNODERM consortium launched its Twitter presence (@INNODERM2020) in December of 2018. Since then, the number of tweets, profile visits and followers have maintained a steady following (Table 2.2.5.1.). The account currently has 141 followers.

Table 2.2.5.1. Twitter statistics since implementation in December 2018.

Month	Tweets	Impressions	Profile visits	New followers
December 2018	1	38	23	2
February 2019	3	749	32	2
June 2020	4	5600	117	-1
July 2021	1	1015	169	1

2.2.6. Other Dissemination Activities

Over the course of the INNODERM project, the consortium members presented project results at more than 100 different occasions, in scientific conferences, summer schools, workshops, interviews, talks, webinars, and press releases.

Table 2.2.6.1. gives an overview of the different dissemination activities. Press releases were distributed through university news outlets and were picked up worldwide by media distribution channels such as ScienceDaily.com, MDTMag.com, ScienceTimes.com, Photonics.com and others. Hundreds of thousands recipients were addressed through these different outlets and significant interest raised in the technology and the INNODERM project.

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Table 2.2.6.1. Overview of the number and types of dissemination and communication activities that occurred during the course of the INNODERM project.

Type of dissemination	Number of events	Audience reached	Partners involved
Scientific conferences	22	Researchers	TUM, ITM
Summer schools	5	Students, researchers	TUM, ITM
Workshops	2	Researchers	TUM
Interviews (radio, TV)	4	General public	TUM
Talks	55	Researchers	TUM
Posters	5	Researchers	TUM, ITM
Webinars	8	Researchers, customers	TUM, ITM
Press releases	5	General public	TUM, Hunimed
Other	5	Researchers, general public	TUM, ITM

3. Summary and Conclusions

In this document we have presented the final report on managing dissemination of results in INNODERM. The success of the project's dissemination efforts is evidenced by many publicly available presentations and publications, some garnering international attention, and can be demonstrated as having a positive impact on the European Community and healthcare industry at large.

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Appendix I: Certificate of top-downloaded article from Wiley Publishing

TOP DOWNLOADED ARTICLE 2017-2018

CONGRATULATIONS TO

Andrei Berezhnoi

whose paper has been recognized as
a top 20 most read paper in

Journal of Biophotonics

WILEY

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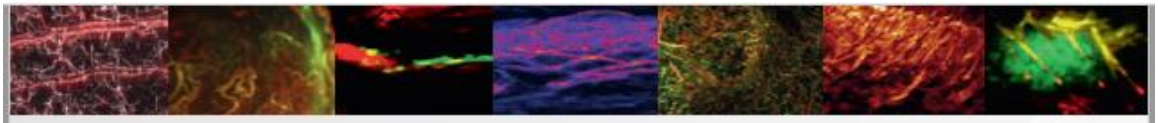


1 iTheraMedical Listening to Molecules

VASODILATION IMAGING

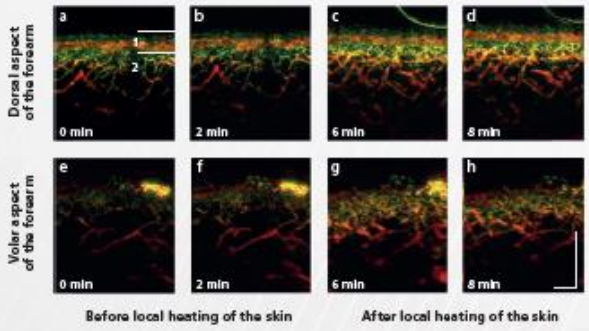
Assessment of vasodilation using raster-scanning optoacoustic mesoscopy (RSOM)

Analysis of skin morphology and microvasculature as well as its response to external stimuli such as heating or pharmacological treatment may reveal vasculature dysfunctions linked to cardiovascular diseases, diabetes, obesity, and metabolic syndrome. Conventional techniques like diffuse correlation spectroscopy/tomography suffer from low signal-to-noise ratio (SNR) and do not provide sufficient resolution to resolve individual microvessels at depth. Other optical methods like laser Doppler perfusion imaging (LDPI) and laser speckle contrast imaging (LSCI) typically characterize only superficial flow as they rely on photons scattered from the surface of the imaged tissue. Furthermore, it has been reported that the repeatability of blood flow measurements using LDPI or LSCI is poor. RSOM has shown a unique ability to visualize skin morphology, including microvasculature, providing intrinsic optical tissue contrast down to 10-20 µm resolution at a penetration depth of several millimeters.

In a recent clinical study, the responsiveness of human skin to local heating was assessed using an RSOM imaging system for exploratory clinical use. In RSOM images, blood volume and single vessel dilation were quantified.

The skin, the largest organ of the human body, is regulated by metabolic and homeostatic processes and is systemically affected by various health conditions. For example, obesity and diabetes are associated with abnormalities in the dermal microvascular bed, reflecting poor skin perfusion and impaired endothelial function [1]. RSOM can visualize microvasculature with a resolution of 10-20 µm resolution, at several millimeters depth without the need for contrast agents, providing spatial information and quantitative metrics that could supplement clinical assessments related to diagnosis and therapy monitoring in skin diseases such as psoriasis [2].

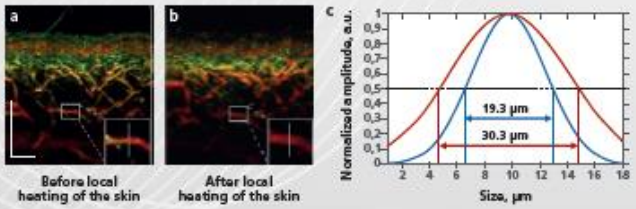
FIGURE 1: RSOM imaging of heat-induced dermal vasodilation



The forearm of a healthy volunteer was imaged before and after heating at 44 °C.
(a-d) Sagittal views of the dorsal aspect of the forearm before and after heating. In panel (a), horizontal lines demarcate the epidermis (1) and dermis (2).
(e-h) Sagittal views of the volar aspect of the forearm before and after heating. Scale bars, 500 µm.

In a recent study [3], an RSOM imaging system was used to image responsiveness of human skin to local heating. RSOM was able to visualize cross-sectional microvascular changes in the skin in the volar and dorsal aspects of the human forearm in response to local hyperthermia.

FIGURE 2: RSOM analysis of hyperthermia in single vessels



(a/b) Sagittal view of the dorsal aspect of the forearm showing the dilation of a single vessel (boxed) before and after heating.
Inset, close-up view of the vessel, with the vertical line indicating the cross-section displayed in panel (c). (c) Amplitude profile of the vessel in panels (a) and (b), before (blue) and after (red) heating. Scale bars, 500 µm.

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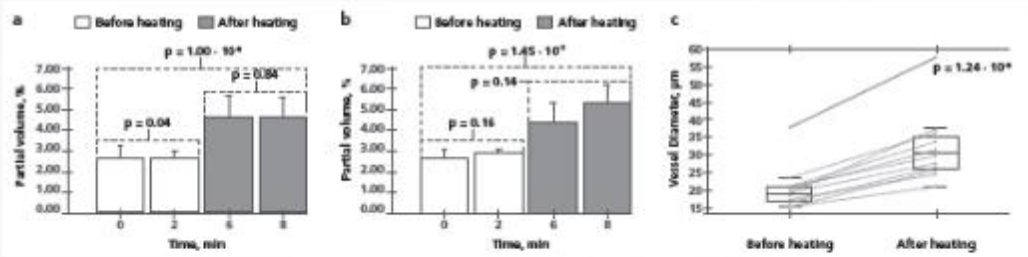
VASODILATION IMAGING 2

Dermal blood volume and vasodilation were quantified based on single-wavelength images obtained at 532 nm. RSOM was effectively used to measure hyperemia in individual vessels. This ability may be valuable for elucidating the poorly understood process of vasodilation and vascular recruitment in non-glabrous skin exposed to focal hyperthermia or other physiological processes and pharmacological interventions.

FIGURE 3: Quantification of RSOM measurements



(a-b) The volar and dorsal aspects of the forearms of six healthy volunteers were imaged using RSOM before and after heating at 44 °C. Partial blood volume was measured in dermis of the (a) volar aspect and (b) dorsal aspect. (c) Blood vessel diameter was measured in 12 arbitrarily selected vessels in the dermal upper plexus of the volar forearm of multiple volunteers. Solid black lines connect diameters of the same vessel before and after heating. p values indicate the significance of the difference between selected samples.

Further work will help to elucidate the physiological mechanism involved in the perfusion changes that can be captured with RSOM.

Conclusions

In conclusion, a recent study has shown that through the use of RSOM it is possible to quantify heat-induced microvasculature changes, providing high-resolution, intrinsic, vascular contrast at several millimeters depth. In the future, RSOM might elucidate thermoregulatory vascular processes that remain poorly understood and may become useful for diagnosis and monitoring of major diseases.

RSOM Imaging Protocol

Imaging System	Repetition Rate	Excitation Wavelength	Processing Methods
RSOM Explorer C50	350 Hz - 1 kHz	532 nm	Multi-bandwidth (11-33 MHz and 33-99 MHz) reconstruction

References

[1] Patik JC et al.,
Impaired endothelium independent vasodilation in the cutaneous microvasculature of young obese adults,
Microvasc Res. 2016 Mar;104:63-8.

[2] Aguirre J et al.,
Precision assessment of label-free psoriasis biomarkers with ultra-broadband optoacoustic mesoscopy,
Nat Biomed Eng, vol. 1, Article number 0068, 2017.

[3] Berezhnoi A et al.,
Assessing hyperthermia-induced vasodilation in human skin *in vivo* using optoacoustic mesoscopy,
J Biophotonics. 2018 Mar 23:e201700359.

The device is for investigational use only.

MKT-3-AN-02 v.1.0

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APPENDIX II: INNODERM PUBLICATION REGISTER

No.	Paper citation reference	Partner(s) involved	Date of publication	WP	Citations
1	M. Talamonti et al., „Role of the HLA-C*06 allele in clinical response to ustekinumab: evidence from real life in a large cohort of European patients“, in British Journal of Dermatology, 2017.	HUNIMED	02/2017	5	42
2	M. Schwarz et al., "Optoacoustic Dermoscopy of the Human Skin: Tuning Excitation Energy for Optimal Detection Bandwidth With Fast and Deep Imaging in vivo," in IEEE Transactions on Medical Imaging, vol. 36, no. 6, pp. 1287-1296, June 2017. doi: 10.1109/TMI.2017.2664142	TUM	03/2017	3	32
3	J. Aguirre et al., “Precision assessment of label-free psoriasis biomarkers with ultra-broadband optoacoustic mesoscopy”, in Nature Biomedical Engineering 1, 0068, May 2017. http://dx.doi.org/10.1038/s41551-017-0068	TUM	05/2017	5	135 (119 Altmetric)
4	A. Narcisi et al. “Listening in to skin disease” in Nature Biomedical Engineering 1, 0076, May 2017 https://doi.org/10.1038/s41551-017-0076	HUNIMED	05/2017	5	0 (7 Alt)
5	M. Schwarz et al. “Motion correction in optoacoustic mesoscopy” in Scientific Reports.	TUM	09/2017	3	32
6	A. Berezhnoi et al. “Assessing hyperthermia-induced vasodilation in human skin in vivo using optoacoustic mesoscopy”, in Journal of Biophotonics, Volume 11, Issue 11, November 2018. https://doi.org/10.1002/jbio.201700359	TUM	03/2018	3	17
7	J. Aguirre et al. “Assessing nailfold microvascular structure with ultra-wideband raster-scan optoacoustic mesoscopy”, Photoacoustics, Volume 10, June 2018, https://doi.org/10.1016/j.pacs.2018.02.002	TUM	06/2018	5	29

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8	B. Hindelang et al. (2018). Non-invasive imaging in dermatology and the unique potential of Raster Scan optoacoustic mesoscopy (RSOM). Journal of the European Academy of Dermatology and Venerology. 1-11. doi:10.1111/jdv.15342	TUM	11/2018	5	19
9	J. Aguirre et al. “Motion quantification and automated correction in clinical RSOM”. IEEE Transactions on Medical Imaging	TUM	01/2019	5	6
10	M. Omar, Aguirre, J., & Ntziachristos, V. (2019). Optoacoustic mesoscopy for biomedicine. Nature Biomedical Engineering. 3 (5). 354-370. doi: 10.1038/s41551-019-0377-4	TUM	04/2019	5	66
11	E Hadjipanayi at el. “In Vitro Characterization of Hypoxia Preconditioned Serum (HPS)—Fibrin Hydrogels: Basis for an Injectable Biomimetic Tissue Regeneration Therapy”, J Funct Biomater. 2019 Jun; 10(2): 22	TUM	05/2019	5	3
12	S. Nitkunanantharajah, et al. (2019). Skin surface detection in 3D optoacoustic mesoscopy based on dynamic programming. IEEE Transactions on Medical Imaging. doi: 10.1109/TMI.2019.2928393	TUM	07/2019	5	22
13	S. Moustadakis et al. " Fully automated identification of skin morphology in raster-scan optoacoustic mesoscopy using artificial intelligence", Med Phys. 2019 Sep;46(9):4046-4056. doi: 10.1002/mp.13725. Epub 2019 Aug 6.	TUM	07/2019	3	10
14	A. Berezhnoi et al. "Optical features of human skin revealed by optoacoustic mesoscopy in the visible and short-wave infrared regions", Optics Letters, Vol. 44, Issue 17, pp. 4119-4122 (2019), https://doi.org/10.1364/OL.44.004119	TUM	09/2019	3	4
15	I. Weidenfeld, et al. (2019). Homogentisic acid-derived pigment as a biocompatible label for optoacoustic imaging of macrophages. Nature communications. doi: 10.1038/s41467-019-13041-4	TUM	11/2019	5	3
16	K. Haedicke et al. “High-resolution optoacoustic imaging of tissue responses to vascular-targeted therapies”. Nat Biomed Eng 4, 286–297 (2020).	iThera (MSKCC)	03/2020	3	25

17	B. Hindelang et al. “Optoakustische Bildgebung–Licht rein, Schall raus?” Aktuelle Dermatologie 4/2020	TUM	04/2020	3	
18	B. Hindelang et al. „Optoacoustic mesoscopy shows potential to increase accuracy of allergy patch testing.” Contact Dermatitis https://doi.org/10.1111/cod.13563 20/4/2020	TUM	04/2020	3	3
19	D. Razansky and Ntziachristos, V. “Optical and Optoacoustic Imaging“ Recent Results in Cancer Research	TUM	06/2020	3	2
20	P. Facheris et al. “Concomitant Pyoderma Gangrenosum-like and Amicrobial Pustulosis of the Folds: a Case Report”. https://pubmed.ncbi.nlm.nih.gov/32648026/	HUNIMED	07/2020	3	3
21	B. Hindelang et al. “Quantification of skin sensitivity to ultraviolet radiation using ultrawideband optoacoustic mesoscopy.”, The British Journal of Dermatology, 29 Nov 2020, 184(2):352-354. DOI: 10.1111/bjd.19463	TUM	11/2020	5	1
22	B. Hindelang et al. “Precision assessment of psoriasis therapy by means of RSOM”	TUM	*In prep*		
23	J. Aguirre et al. “Precision light based selective thermomechanical coagulation in tattoo removal using optoacoustic mesoscopy”	TUM	*In prep*		

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