INNODERM

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D5.3: SECOND REPORT ON MICROSCOPY IMAGING FEATURES IN SKIN DISEASES

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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. PURPOSE OF THIS DOCUMENT

In this document, we show the latest advancements and results of the INNODERM microscopy imaging campaign. In previous trials, it was determined that the RSOM would act as a stand-alone device, and further development of RSOM^2 would not be pursued. In that regard, we report only results from the RSOM^2 instrumentation proof of concept. As this is a public deliverable, only those results which are already published and available through open access journals.

2. RSOM CAN OFFER SCALABLE RESOLUTION FOR MICROSCOPY AND MESOSCOPY

Optoacoustic imaging provides scalable resolution at microscopic and mesoscopic depths that could uniquely provide comprehensive information on surface capillaries and vasculature, which may further link to inflammatory and cancer conditions.

A hybrid and portable optoacoustic microscopy and mesoscopy set-up enabling highly scalable imaging was developed. The proposed design utilized a customised focused broadband transducer along with fibre-based focused illumination in a confocal arrangement. The system was designed to operate with a secondary diffuse illumination path for mesoscopy. Figure 2.1 shows the optical resolution optoacoustic microscopy (OR-OAM), which integrates the RSOM and RSOM^2 imaging prototypes developed during INNODERM.

We used mouse ears to assess the *ex vivo* and *in vivo* imaging capabilities of the proposed OR-OAM setup.

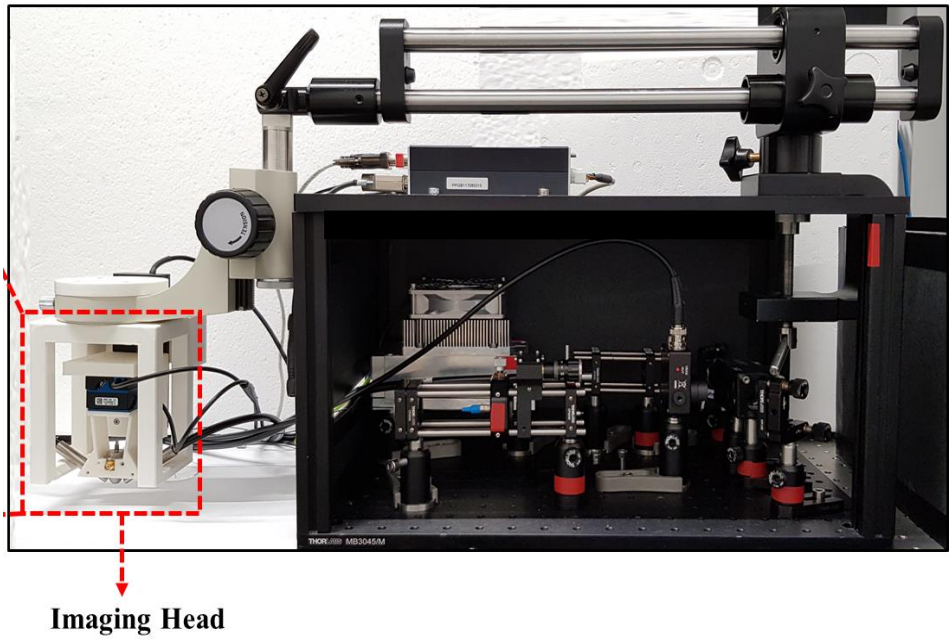

Figure 2.1. Optoacoustic microscopy and mesoscopy imaging setup developed during the INNODERM project.

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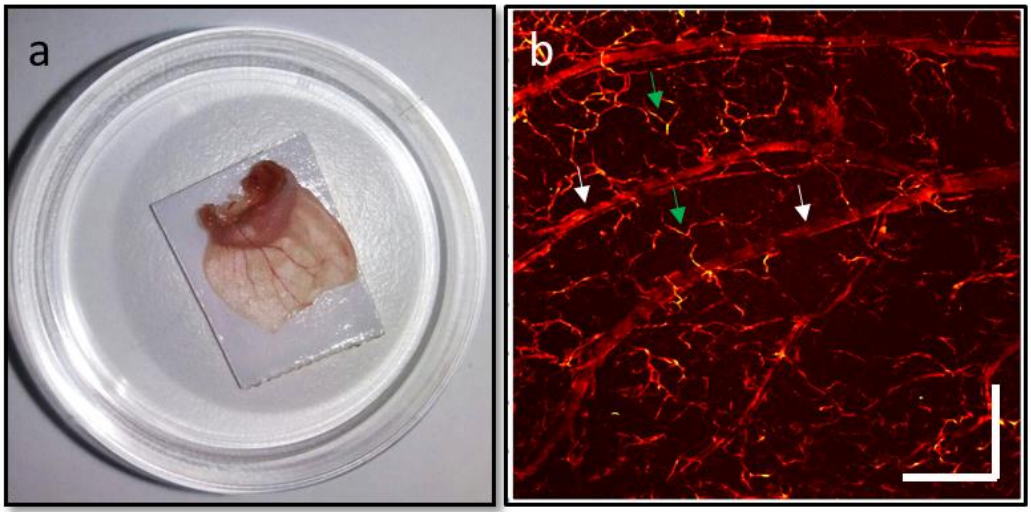

Figure 2.2. (a) Excised mouse ear. (b) OR-OAM microscopy image of the excised mouse ear. The white arrows point at the bigger arterioles and venoules, while the green arrows point at the smallest capillaries. Scale bar is 120 µm.

The confocal configuration enabled artery, vein and capillary imaging in great detail in excised (*ex vivo*) mouse ear (Figure 2.2.). Encouraged by these results, we tested the imaging performance of the system by *in vivo* scanning the ear of 8-week old female Hsd:Athymic Nude-Foxn1nu mice. Figure 2.3. (b-d) shows the anatomical landmarks corresponding to microvasculature of the mouse ear, including arterioles, venoules, and capillaries.

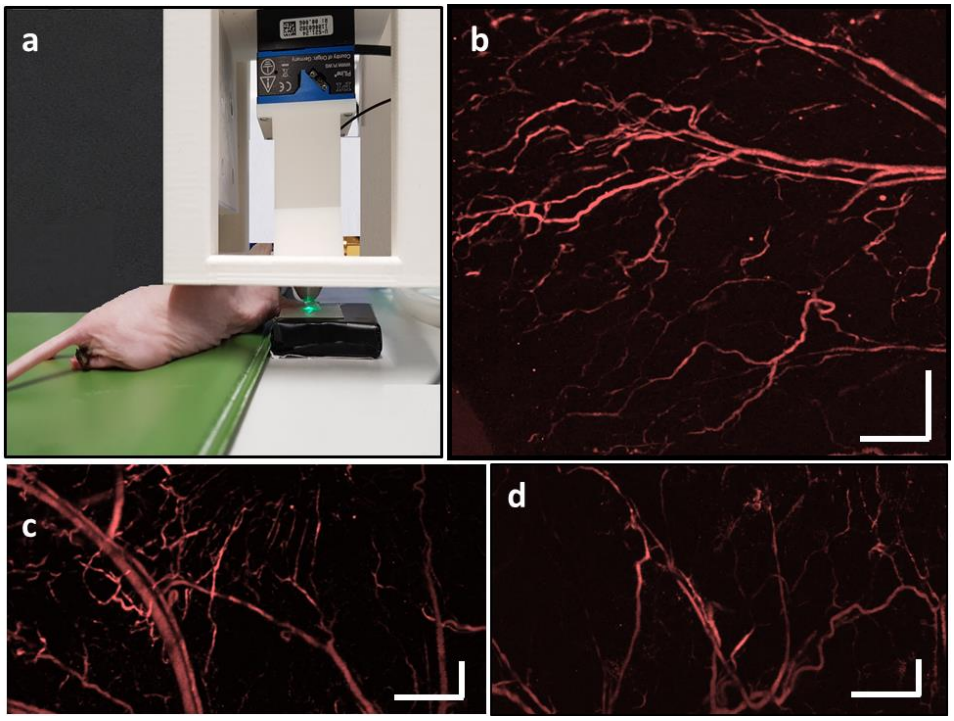

Figure 2.3. In vivo mouse ear optoacoustic microscopy imaging. (b-d) Optical resolution optoacoustic images of the mouse ear.

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Similar to the experiments performed for optoacoustic microscopy (RSOM^2), the optoacoustic mesoscopy performance was tested *in vivo* in a mouse ear. In Figure 2.4, we show the hybrid image with both microscopy and mesoscopy views. Arrows indicate the arterioles-venoules revealed, with superficial but highly resolved small capillaries shown in microscopy mode (green arrows) and deeper big arterioles and venoules revealed in mesoscopy mode (white arrows).

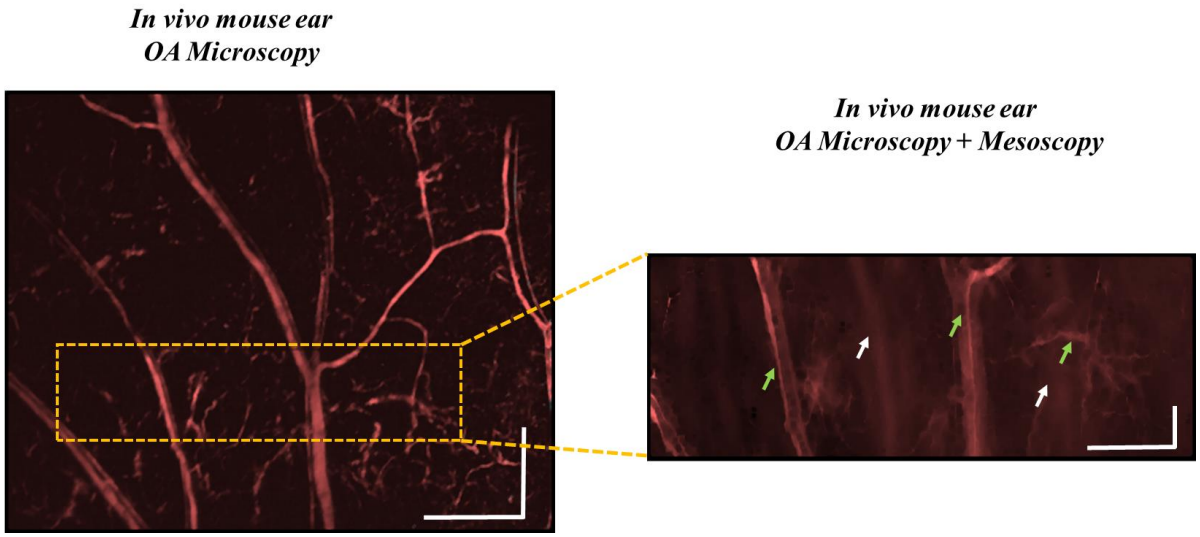

Figure 2.4. Top view optoacoustic microscopy and mesoscopy image of the mouse ear taken in-vivo. (a) Optical resolution microscopy Image. (b) Microscopy and mesoscopy image of ROI. The green arrows point at the big arterioles-venoules and the small capillaries, which are taken with microscopy, while the white arrows point at the deeper, larger arterioles and venoules, which were obtained with mesoscopy.

Our integrated confocal configuration approach demonstrated the possibility to combine high frequency transducers with central illumination using a fibre lens and diffuse illumination with a fiber bundle. This reveals high lateral resolution and sensitivity image visualization of both the superficial microvascular network at high resolution and deeper vasculature in the mouse ear. We expect this ability to assist in the study of microvasculature changes (e.g., angiogenesis) within different skin plexus for clinical application.

3. Conclusions and Future Plans

Here, we have presented Deliverable 5.3, which is an updated, public version of the information enclosed in Deliverable 5.2., reporting results from the RSOM^2 instrumentation proof of concept.

We have shown microscopy imaging features that were detected using a hybrid scale optoacoustic imaging system combining mesoscopy and microscopy and demonstrated that

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OR-OAM enables high lateral resolution and sensitivity to investigate optoacoustic biomarkers and visualize superficial and deeper vascular structures within the skin. However and as is described in the confidential technical report and in forthcoming publications, the RSOM can act as a stand-alone device, able to perform microscopy imaging without the need for RSOM^2 or an integrated OR-OAM device. For this reason, further development of RSOM^2 and hybrid device was not carried out beyond what is described in this deliverable.

The team will continue to work on additional RSOM^2 development in the future, but until significant performance improvements can be achieved and clear clinical benefit over RSOM demonstrated, the exploitation efforts for RSOM^{2}will remain on hold.

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