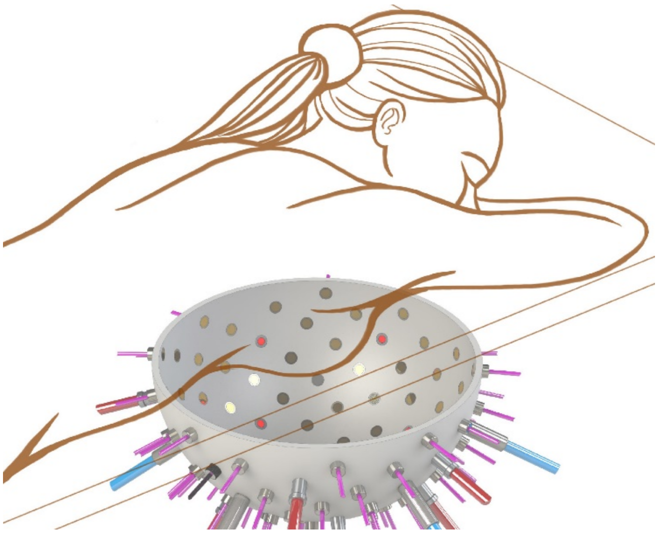
PAMMOTH

Photoacoustic/Ultrasound Mammoscopy for evaluating screening-detected lesions in the breast



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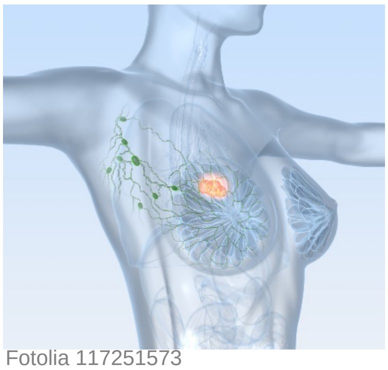
PAMMOTH publishable summary

January 2020

Content

PAMMOTH – publishable summary

PAMMOTH is a collaborative research project, receiving a 5.1 Mio € grant from the European Commission and the Swiss Government in the H2020 research and innovation program. Having started in 2017, within four years, experts from seven countries develop a novel system that uses light and sound to provide a more accurate diagnosis of breast cancer.



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The PAMMOTH project on 'Photoacoustic Ultrasound Mammoscopy for evaluating screening detected abnormalities in the breast', hopes to lead the research into photoacoustic real-time 3D imaging of suspicious lesions. Project coordinator Srirang Manohar, University of Twente, explains: 'We are creating an imaging device that we hope will reduce all of the stages involved in spotting breast cancer into one convenient appointment in order to reduce time, uncertainty and the number of unnecessary biopsies. We intend to make breast cancer diagnosis 'a one-stop-shop, while you wait.'

Summary of the context and overall objectives of the project

With Europe's aging population, its high incidence of breast cancer, its tightening health-care budget, [Rechel *et al* 2013, Ferlay *et al* 2013, Karanikolos *et al* 2013, Morgan & Astolfi 2015] and drawbacks in conventional breast imaging modalities, [Nass, S.J. *et al* 2001] **there is a need for a technique that can provide imaging with high specificity, contrast and spatial resolution, all at a sufficiently low cost** that it can be made universally available. Photoacoustic (also called optoacoustic) imaging [Wang & Hu 2012, Beard 2011, Ntziachristos & Razansky 2010], in which the contrast is dependent on light absorption and which therefore offers spectroscopic (molecular) specificity, has the potential to be that technique [Heijblom et al 2015a]. However, while the literature of the last 15 years has witnessed technological advances in photoacoustic breast imaging, these have been incremental and conservative steps, fragmented across various groups and companies. The end result is that many possibilities and opportunities have not been exploited or explored, and even after a decade and half following the first application of photoacoustic imaging in the breast, [Oraevsky et al 2001] we still describe the method tantalizingly as having potential and promise.

PAMMOTH brings together applied physicists, technology developers, mathematicians, algorithm developers, ultrasound detection experts, laser specialists, epidemiologists and radiologists to work on a new generation system for imaging the breast using both photoacoustics and ultrasound. Academia, Industry and the Clinic from 6 different countries form a strong European consortium in PAMMOTH.

The PAMMOTH consortium's objective is to **develop, validate and begin exploitation of a dedicated breast imaging device for a significant impact in breast cancer diagnosis.** The proposed device combines **non-invasive 3D photoacoustic imaging and ultrasound imaging.** The device will provide **full-breast, multimodal images** to the radiologist. From the ultrasound mode, the radiologist will visualize **anatomical features and extent of tumors**, and from multiwavelength photoacoustics, she will see tumor vascularity. Quantitative spectroscopic photoacoustic images will be extracted off-line, providing the radiologist information relating to **tumor physiology and function such as angiogenesis and hypoxia.**

The choice of the relevant biological targets, and of the functionalities and technical principles applied in the PAMMOTH imager, will provide relevant information to the radiologist to **make accurate diagnosis with high specificity.**

The consortium aims to make the imaging device *for all populations of women, with short time intervals between positive screening and diagnosis. The device has high through-put, possesses no carcinogenic potential and causes no pain and discomfort to patients.*

Work performed from the beginning of the project to the end of the period

At the 36th month in the project we have together realized the following:

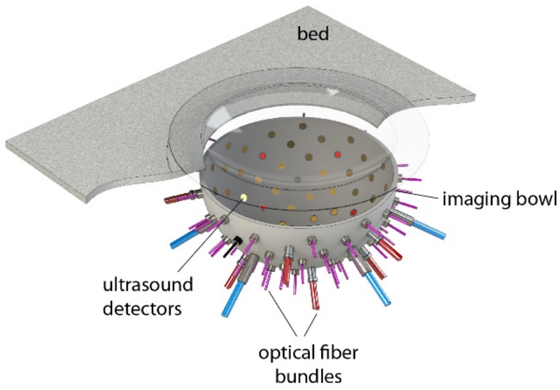
- The clinical prototype PAMMOTH, boasting sub-systems that are technically beyond the state-of-the-art, has been developed and installed in the Medisch Spectrum Twente Hospital, Oldenzaal. The system underwent tests and a risk management report evaluating the risks due to electrical, mechanical, hygienic, ultrasound, and laser control aspects of the imager was developed. This has been submitted to the Medical Ethical Review Committee along with the study protocol. An improved study protocol was re-submitted and approval for the start of the human subject study is awaited.
- The developed ns laser has among the highest energy outputs per pulse compared with lasers for the same applications. The OPO pumped by the laser allows fast tuning and high efficiency. The light is coupled to the PAMMOTH imager using an optical fiber bundle, designed to accept high energy pulses, split in 40 outputs.
- The 512 ultrasound transducer elements arranged in hemispherical geometry provide a low minimum detectable pressure with a wide fractional frequency bandwidth.
- The 512 multi-channel Data-Acquisition System (DAS) is also equipped to transmit ultrasound from the same transducers for ultrasound imaging.
- Cups of various sizes to immobilize the breast during measurements have been produced to hold the breast in the imaging bowl.
- A novel algorithm has been developed for the specific task of reconstructing intermediate images on the fly as projections are being acquired.
- Novel algorithms for speed of sound reconstruction from ultrasound data have been developed and tested.
- A photoacoustic image reconstruction (using an a priori known speed of sound map) based on an iterative approach has been developed.
- The algorithm for quantitative photoacoustic reconstruction has been developed.
- The framework for automatic planning and execution of the off-line image reconstructions (quantitative photoacoustics) has been implemented.
- A suite of test and calibration objects has been developed. Further, a novel 3D phantom simulating both acoustic and optical properties of the breast and its abnormalities has been developed for studying the performance of the system. This phantom also carries blood vessel simulating channels through which blood can be streamed, whose oxygen saturation can be controlled.

Progress beyond the state of the art and expected potential impact

(including the socio-economic impact and the wider societal implications of the project so far)

- The combination of quantitative photoacoustic and ultrasound imaging makes the PAMMOTH imager unique.
- The laser developed produces pulse energies at the fundamental and second-harmonic which are highest for lasers used in the same class of applications.
- The characteristics of the ultrasound detectors are superior to the state-of-the-art detectors.
- A multi-channel Data-Acquisition System (DAS) shows low noise and also has higher level of complexity compared to devices available. The analog front ends in the PAMMOTH DAQ are also capable of driving ultrasound generation by electrical actuation of transducers.
- The ultrasound simulation codes required for the acoustic inversion were optimized for systems with multiple GPUs reaching almost 10-fold speed-up compared to conventional servers.
- The 3D phantom developed are among the first for photoacoustics which may be described as semi-anthropomorphic as well as physiopathological phantoms.

PAMMOTH concept



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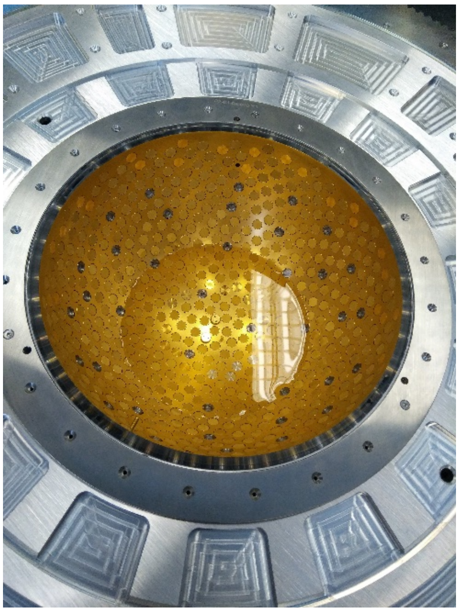
Imaging bowl in the PAMMOTH realization



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Public website

More information on PAMMOTH is available via www.pammoth-2020.eu. The public PAMMOTH website addresses the wider public, presents PAMMOTH's research and technical objectives, explains partners' complementary expertise – also as videos - and will be dynamic and continuously be updated. Training and further information material is available via https://www.pammoth-2020.eu/online-training.html.

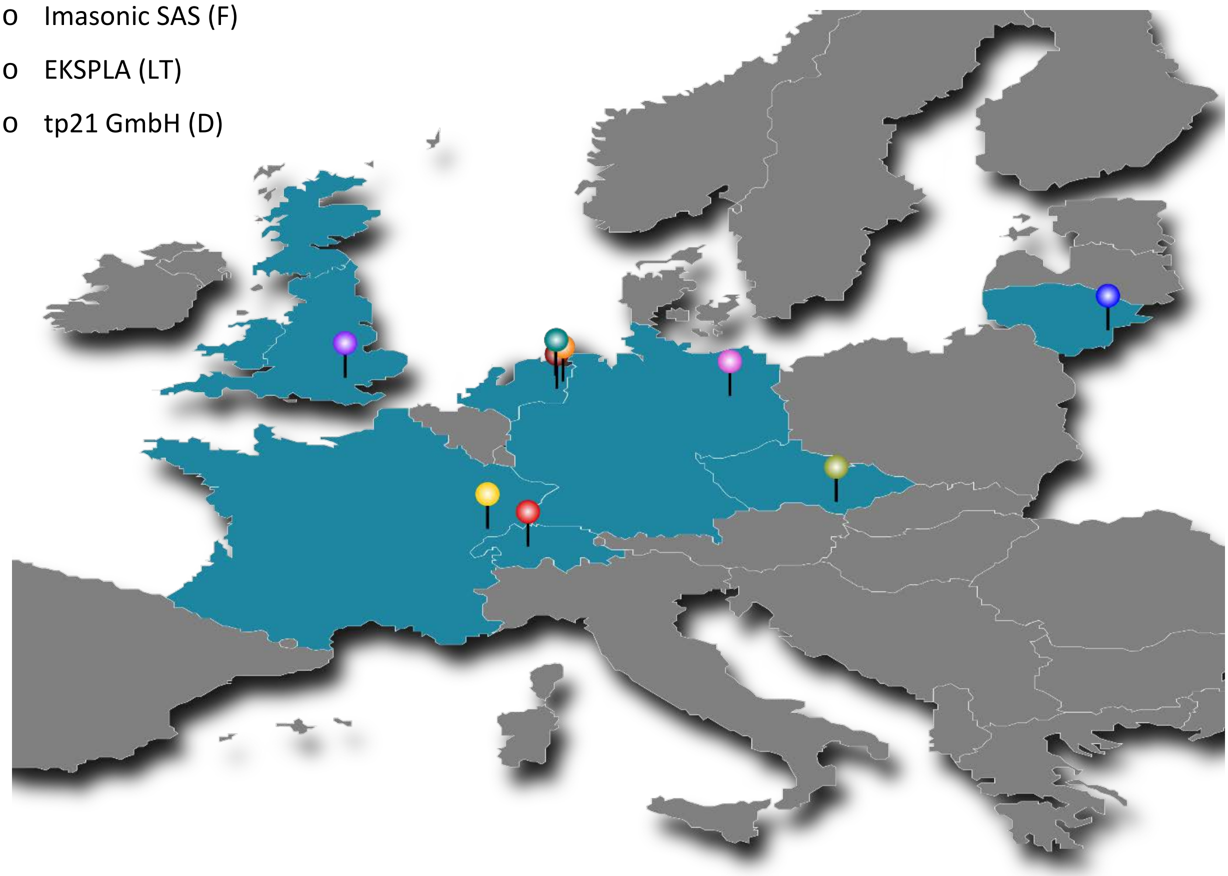
PAMMOTH - consortium

Coordinator

- University of Twente (NL)

Partners

- PA Imaging R&D B.V. (NL)
- Stichting Medisch Spectrum Twente (NL)
- University College London (UK)
- University of Bern (CH)
- Brno University of Technology (CZ)
- Imasonic SAS (F)
- EKSPLA (LT)
- tp21 GmbH (D)



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PAMMOTH is part of the European Technology Platform Photonics21, founded in 2005, representing the industry as well as research organisations in the field of photonics in Europe.