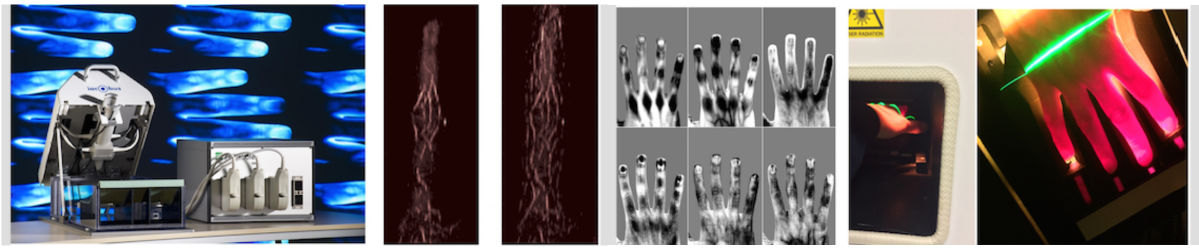

Publishable summary

of the 1st period activities and results

Grant Agreement Number: **305760**

Project acronym: **IACOBUS**

Project title: Diagnosis and Monitoring of Inflammatory and Arthritic diseases using a COmbined approach Based on Ultrasound, optoacoustic and hyperSpectral imaging

Period covered: from **01.01.2013** to **30.06.2014**

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Publishable summary – period 1

Project context and objectives

Arthritic diseases, including rheumatoid arthritis, psoriatic arthritis and osteoarthritis, have a prevalence between 2 and 3% and lead to joint destruction and deformation resulting in a loss of function. The joints of the fingers and hands are frequently affected, and progression of the arthritic disease severely affects the patients' quality of life. Different studies on rheumatoid arthritis have shown that a therapeutic window of opportunities exists in the first year and particularly in the first 3 months after the onset of the disease, during which a treatment has a higher likelihood for improving the course of this devastating disease. However, currently available diagnostic imaging tools are poorly suited to detect early signs of arthritic inflammation. Available diagnostic modalities such as ultrasound, Doppler, MRI or X-ray are either not sensitive enough or not suitable for repeated screenings due to the use of ionizing radiation or high costs.

In order to make use of this window of opportunity, the FP7 funded project IACOBUS has been launched on January 1, 2013 with the goal of making available a new tool dedicated to diagnosis of early arthritis symptoms in fingers joints. In IACOBUS, a European research consortium coordinated by the Fraunhofer Institute for Biomedical Engineering (Fraunhofer IBMT) is developing a new multimodal imaging system which will facilitate the early diagnosis of arthritis affecting the hands. Fraunhofer IBMT possesses more than 25 years of experience in the field on non-invasive imaging methods especially ultrasound and optoacoustic technology. For the IACOBUS approach, the project partners NTNU and NEO will develop a hyperspectral imaging system for overview scanning of the hands and identifying potential sites of joint inflammation. In a second step, a high-resolution 3D joint imaging platform will be developed by the project partners Fraunhofer IBMT, EKSPLA and Vermon. They will develop a system combining optoacoustic and ultrasound imaging allowing a detailed investigation of the inflamed joints identified by the hyperspectral imaging tool. Opto-acoustic imaging is a functional technology using laser-generated acoustic waves for visualizing the internal structures of soft tissue and therefore opens a broad field of applications in clinical assessment as well as serving as research tool in basic life sciences.

Work performed and the main results

Since the beginning of the project, the technology partners Fraunhofer IBMT, EKSPLA, VERMON, NTNU and NEO have worked in close cooperation with the clinical partner Justus-Liebig-Universität on the development of the proposed multimodal imaging systems. After a specification definition phase, the partners NEO and NTNU have started the development of a hyperspectral imaging system suitable for usage in a clinical setting. At first, an ideal spectral range for in-vivo measurements has been identified. Preliminary experiments have shown that the most promising spectral region lies between 600 nm and 1200 nm where high contrast between different tissue constituents could be achieved. In a second step, an overall optical system was designed. This included both the identification of a high sensitivity sensor covering the above mentioned spectral range and the design of a mechanical system allowing to acquire 3D hyperspectral datacubes with a 2D sensor having one spatial and one spectral dimension. The concept of the whole imaging module was designed following ergonomics principles and emphasizing on ease of access and functionality at the clinic. Finally, a pretrial was performed at St. Olavs Hospital during which three parameters could be identified as potential indicators of arthritic diseases in finger joints: Vasculature density, blood content and transmission. The development of the ultrasound/optoacoustic (US/OA) system has been performed by the partners EKSPLA, FRAUNHOFER IBMT and VERMON. Conventionally, industrial or scientific laser systems are used for signal generation in optoacoustic imaging tasks. However, such systems are mostly poorly suited for a use in a clinical environment due to their low repetition rate limiting the achievable image rate, their large size or their low energy level. For this purpose, EKSPLA has designed the IACOBUS laser with special focus on features affecting the user comfort in an optoacoustic imaging setting. For instance, the OPO has been built in a compact shoe box design and a pulse repetition rate of 100 Hz has been achieved. Furthermore, diode pumping has been implemented which allows higher efficiency and lower acoustic noise level. With respect to the acoustic components of the system, VERMON and FRAUNHOFER IBMT have designed a probe with more than 700 individual elements allowing tomographic imaging of all finger joints. The concept is based on a tomographic probe consisting of four 90° arcs which are scanned in elevational direction for acquisition of 3D data. For signal acquisition, VERMON has developed 10 MHz cMUT arrays with corresponding preamplification and impedance matching circuitry. Preliminary tests have shown the superior bandwidth and sensitivity of VERMON´s cMUTs when compared to conventional ultrasound detector based on piezoelectric transducers. For digitization and data preprocessing, FRAUNHOFER IBMT has developed a new multichannel electronics platform allowing the acquisition of signals from 128 transducer elements simultaneously. In order to be usable with high frequency transducers, a sampling frequency of 80 MSamples/s has been realized. Furthermore, the device allows fast switching between optoacoustic and ultrasound mode and supports data transfer with the latest high speed protocols such as PCI express. Thereby, acquired signals can be transferred to personal computers where signal processing, reconstruction (beamforming) and visualization tasks can be performed highly parallelized in Graphical Processing Units (GPU). This flexible concept based on software processing of ultrasound data allows easy integration of new algorithm types and taking full profit of the increasing performance of upcoming GPU generations. Finally, FRAUNHOFER IBMT has developed a multiplexing concept allowing to drive VERMON´s 768 element tomographic probe with the 128 channel electronics platform. In addition to the hardware developing tasks, the development of adequate algorithms for image reconstruction, signal processing and parameter extraction has been in the focus of the IACOBUS research activities. For instance, NTNU has developed a robust collection of algorithms for identifying tissue constituents and related parameters using a real time analysis methodology and FRAUNHOFER IBMT has developed a novel approach for calibration of (opto)acoustic tomographic imaging systems.

Expected final results and their potential impacts and use

In the first 18 months of the IACOBUS project, the required components allowing the implementation of hyperspectral and optoacoustic/acoustic imaging devices dedicated to the task of finger joint imaging have been developed and at least partially been tested under laboratory conditions. The full capabilities of the approach and its impact on the clinical community and beyond will however only be assessable once the systems are fully integrated and validated in realistic scenarios. However, based on the current status of the project and the evaluation made so far in preliminary trials (hyperspectral imaging) and in phantom tests (optoacoustic and acoustic imaging), the expected final results can be extrapolated. Preliminary proband experiments have shown that diagnostically relevant parameters such as vasculature density, blood content and transmission can be retrieved non-invasively in real time using hyperspectral techniques. Since hyperspectral imaging is a low-cost technology, it could be used for screenings in risk patient groups and lead to earlier detection of the disease. This would allow to really take advantage of the well-know “therapeutic window of opportunities” in the first three months after the onset of the disease. Consequently, this would help to prevent both the devastating long-term consequences for the patients (pain, loss of finger function, inability to work) and the high disease-associated costs (ranging from 11.000 to 16.000 € indirect costs per patient and per year). Preliminary experiments with the available optoacoustic components have furthermore shown the superior sensitivity of the proposed technique based on cMUT detectors. Since optoacoustic signal amplitudes directly scale with absorption, an enhanced sensitivity means that smaller vessels (having smaller volumes) can be detected. The developments in the field of optoacoustic imaging will therefore help to bring this technology closer to a routine use in the clinical field. Furthermore, the design of the US/OA is based on an automated 3D scan of fingers which will overcome the main backdraw of Doppler ultrasound as diagnostic tool for arthritic inflammation (high level of inter-user variability, intensive training needed). This will as well allow to perform routine scans for earlier diagnosis of the disease. The project will furthermore have an impact on the research community since it will foster activities in the field of molecular imaging. For instance, when combined with suitable (functionalized) contrast agents, the devices can be used for investigation of the EPR effect both on the macroscopic (hyperspectral) and microscopic (US/OA) level. The dimensions of the US/OA device will further allow to address the market of small animal research equipment where non-invasive diagnostic tools being in compliance with the 3R strategy are of highest relevance.