1. Publishable summary

Project context and objectives

In recent years MR-guided focused ultrasound surgery (MRgFUS) has become a frequently applied means for the treatment of fibromyoma of uterus and of bone metastases. MRgFUS combines high intensity focused ultrasound for thermal ablation of diseased tissue with MR imaging to visualise the tumour and surrounding anatomy and to provide MR thermal feedback.

Treating tumours in moving organs with MRgFUS however presents tremendous technological challenges including motion due to breathing and shielding of the target by the rib cage. The VPH project FUSIMO (2011-2014) aimed at the development of a planning system for MRgFUS capable to deal with the challenges in the treatment of moving abdominal organs.

TRANS-FUSIMO will translate the FUSIMO results into a clinically applicable system spanning the full clinical workflow of planning, conducting and assessing as well as learning from the procedure. With such an integrated system, MRgFUS can become a commercially and clinically competitive alternative to current surgical and minimal-invasive oncological interventions, thus providing a non-invasive treatment, reducing side effects and healthcare costs. The particular objectives for the TRANS-FUSIMO project are:

- Development of TRANS-FUSIMO treatment system to support conducting and assessing of the intervention under breathing motion,
- Interfacing state-of-the-art FUS hardware and imaging devices to build an integrated real-time-capable system for liver FUS,

TRANS-FUSIMO – Clinical Translation of Patient-Specific Planning and Conducting of FUS Treatment in Moving Organs

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University of Dundee (United Kingdom) – UNIVDUN

Stiftelsen SINTEF (Norway) – SNF

Eidgenössische Technische Hochschule Zürich (Switzerland) – ETH

Medical Imaging Research Institute Mediri (Germany) – MED

IBSmm Engineering (Czech Republic) – IBSMM

InSightec Ltd. (Israel) – INS

GE Medical Systems Ltd. (Israel) – GE

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Johann Wolfgang Goethe Universitaet Frankfurt (Germany) – UOF

Universita Degli Studi Di Palermo (Italy) - UOP

Timetable:

January 2014 to December 2018

Total cost: € 5,601,915.00

EC funding: € 4,049,999.00

- Improving model components for optimized clinical workflow, real-time applicability and validated outcome prediction,
- Allowing training and learning using the TRANS-FUSIMO software system by building a case and results database,
- Conducting of pre-clinical (phantoms, cadaver, animal) experiments with the TRANS-FUSIMO system.

In a clinical trial, the feasibility of using the TRANS-FUSIMO treatment system for neoadjuvant MRgFUS to achieve prolonged survival will be investigated.

The main emphasis of the TRANS-FUSIMO project lies on the implementation and validation of a real-time control system that is able to control the following hardware devices:

- MR hardware for acquisition of anatomical and thermometry data,
- FUS hardware for generating and focusing high intensity ultrasound,
- US and MR imaging for tracking the movement of liver and ribs,
- Robot arm for placement of the ultrasound transducer on supine patients.

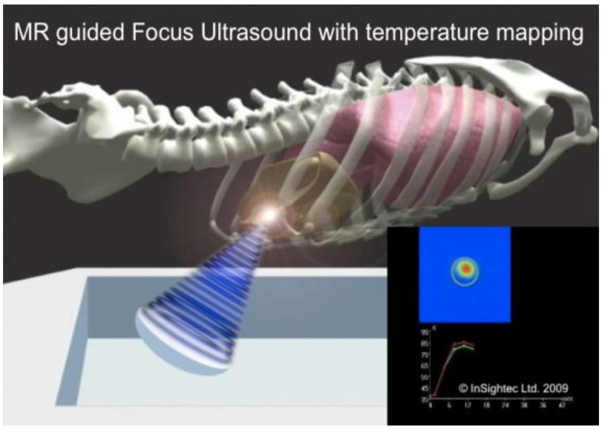

Figure 1: Ilustration of abdominal FUS

With the real-time interfacing of the MR hardware the TRANS-FUSIMO treatment system is able to receive real-time images from the MR device. There are several time points during the treatment process where images from the MR are needed but which do not necessarily need to be transferred in real-time, namely the planning images and the transducer calibration images. Only the monitoring images are needed in real-time which on the one hand show the motion of the breathing patient in order to receive information about the moving target as accurate as possible and on the other hand to get real-time information about the rising temperature in the body during sonication. Another possibility to track the target area is to use a diagnostic ultrasound device with real-time capability. With this information and a statistical motion model extended in TRANS-FUSIMO, the steering of the FUS hardware can be performed. Thus, the TRANS-FUSIMO treatment system has also the ability to communicate real-time motion information to the steering server provided by the FUS hardware company InSightec. The last hardware component is the robot arm which will put the transducer in place at the beginning of the procedure and which has a separate interface for the user.

After finishing the hardware adaptations, the TRANS-FUSIMO project performs preclinical in-vitro and ex-vivo tests as well as an animal study. In a later stage of the project a first patient study will be conducted with patients under breathhold, i.e. without breathing motion. In the last phase of the project a clinical trial with patients that are treated with MRgFUS under breathing motion will be conducted.

To allow clinical personnel to train and learn MRgFUS therapy and the TRANS-FUSIMO treatment system, a training and learning system is implemented which uses emulated hardware devices and data that has been recorded during real interventions. This training will be available outside of the

MRgFUS therapy room to learn how to perform a proper therapy with the TRANS-FUSIMO treatment system.

Work performed and main results

In the first two years of the TRANS-FUSIMO project the consortium was focussing on developing the TRANS-FUSIMO treatment system which enables an MRgFUS therapy in the liver. Compared to the work performed in the FUSIMO project, which showed proof of concept for MRgFUS therapy of the liver, the TRANS-FUSIMO treatment system shows major differences: It integrates all requirements on the therapy execution in one software which can be used in a systematic way by all partners:

- Real-time communication with MR device
- Real-time communication with FUS device
- Integration of MR tracking algorithm
- Integration of linear motion prediction methods.

In the second project year (=reporting period for the present document), a first version with all integrated interfaces was tested in-vitro. The parameters to be validated were defined according to safety provisions. This validation represents a large part of the quality assurance, which is needed to use the TRANS-FUSIMO treatment system in in-vivo studies.

The complex motion model was largely extended during the first two years of the project. During FUSIMO it was necessary to mark specific points in the liver to transfer the new case to the generic motion model atlas. This was changed in TRANS-FUSIMO by using a shape model of the liver which facilitates the usage of the complex motion model. Furthermore, the simulation of the therapy was improved and extended to also simulate various focussing methods which take risk structures like ribs into account.

In addition to the already mentioned outcomes, there are two results which directly relate to improved applicability of an MRgFUS treatment: The positioning of the FUS device is sometimes very difficult, thus, an interface to a robotic arm was implemented which can facilitate the placement. On the other hand, a training and learning system was developed helping the physicians to use the newly developed TRANS-FUSIMO treatment system and to replay and learn from the last performed procedures.

The main clinical result in the last period had been the approval of the animal pilot study at the new partner University of Palermo who accessed the project in January 2015. Also, several ethical approvals for the scanning of volunteers were submitted and approved.

To raise awareness for the research topic and the TRANS-FUSIMO project in particular and to build links to the scientific community, dissemination activities play a particularly important role for the TRANS-FUSIMO project. Therefore, several contributions to international conferences and workshops have been made. Also, the public website has been improved and the project has been featured on Twitter. In scientific sessions, dedicated symposia and exhibition booths of several congresses in the field, the TRANS-FUSIMO project has been presented to the scientific medical-radiological and technical-engineering communities. The main results in the second period was on the one hand a booth at the ICT 2015 conference organized by the European Commission where scientists as well as representatives of the industry have visited the booth and learned about the TRANS-FUSIMO project. On the other hand, a contact was established to the EU projects FUTURA and GoSmart. FUTURA and TRANS-FUSIMO shared a booth at the CIRSE conference which was also visited by industry representatives. The contact to GoSmart was based on scientific aspects related to a publicly available pig CT database which TRANS-FUSIMO now also partly uses for a liver shape model of pigs.

Expected final results and potential impact

The expected outcome of the TRANS-FUSIMO project is a prototype for a treatment system for MRgFUS procedures in moving abdominal organs, especially in the liver. The system will be validated during a preclinical animal trial and a clinical trial. In combination with the FUSIMO demonstrator as a planning tool and a training and learning tool, TRANS-FUSIMO covers the whole pipeline for MRgFUS liver interventions: new clinical personnel is able to train such procedures by means of previous cases, actual cases can be planned and a real-time treatment system enables the physicians to treat the patients during free breathing.

The long-term impact of TRANS-FUSIMO lies in improving the treatment of cancer and metastases in a variety of organs and for a wide range of patients. This will contribute to substantially reducing the estimated 1.7 million deaths in Europe each year. The reduced side effects (compared to conventional surgery, systemic chemotherapy and radiation therapy) of the MRgFUS will reduce complications and consequently lead to a higher quality treatment of the patients at lower financial demand for health insurance and social welfare.