Mid-term report

Heterogeneity correction for large aperture HIFU transducers for improved breast cancer ablation

I. HYPOTHESIS OF THE PROJECT

The risk of undesired tissue damage to thoracic cage, heart and lung during MR guided HIFU ablations of breast cancer can be greatly reduced if transducer design with a lateral beam direction is used in combination with a large aperture. The resulting increase of tissue heterogeneity will induced focus aberrations that can be corrected phase corrections based on high resolution MRI measurements.

II. SPECIFIC AIMS

The proposed project combines high resolution MRI with in-vivo celerity measurements of different breast tissue types [1] to develop an automatic phase correction method which compensates for tissue imposed focal point aberrations. Since MR guided HIFU ablations of breast cancer already use MR anatomical images for treatment planning, this correction method will not require any additional imaging modality and can be integrated in a time effective and seamless way in current therapy protocols.

SUMMARY OF MEASURABLE RESULTS FOR THE ENTIRE PROJECT

- Experimental comparison of the accuracy of the phase correction based on hydrophone measurements to the model based corrections computed from MRI and celerity data.
- Quantitative analysis of the typical energy dispersion induced by inhomogeneous breast tissue when a lateral firing HIFU-system is used (expressed in FWHM increase, miss registration and loss of peak amplitude of the acoustic pressure field in the beam focus).
- Technical demonstration in a phantom of a clinically feasible (scan duration <10min) MRI protocol, which in conjunction with a priori knowledge of the breast tissue celerity allows to refocus the aberrated beam of a lateral firing HIFU-system to 80% of its original peak amplitude of the acoustic pressure field in the beam focus.
- Quantitative prediction of the expected improvement of such a technique in a clinical ablation scenario based on ex-vivo experimentation and acoustic simulations.

QUARTERLY RESEARCH GOALS AND DELIVERABLES:

1	• Deployment of a lateral beam-path HIFU-system. • Installation of a 3d hydrophone setup with tailored software for precise acoustic beam characterization. • Construction of a breast phantom with similar acoustic properties and bNMR characteristics than human breast tissue. • Development of a 3d MRI sequence for tissue characterization.
2	• Characterization of the focal point shape in a homogeneous propagation medium. • Characterization of the focal point shape in the inhomogeneous breast phantom. • Development of the phase correction algorithm for acoustic beam shaping based on the 3d MRI data.
3	• Refocusing (beam shaping) of the focal point in the inhomogeneous Breast phantom based on direct acoustic measurements.
4	• Refocusing (beam shaping) of the focal point in the inhomogeneous breast phantom based on MRI data and the acoustic modeling.

DELIVERABLES Q1:

DEPLOYMENT OF A LATERAL BEAM-PATH HIFU-SYSTEM

The project was conducted with a dedicated Sonalleve breast HIFU system (Philips Healthcare, Vantaa, Finland) which uses a large aperture transducer system (240° opening angle, focal length 13cm) composed of 256 channels working at 1.45MHz. Due to manufacturing constraints of such large aperture transducer design, it was composed of 12 separate modules, each consisting of 32 elements of 6.6 mm diameter. However for the described study only 246 elements, distributed over 8 modules, were used.

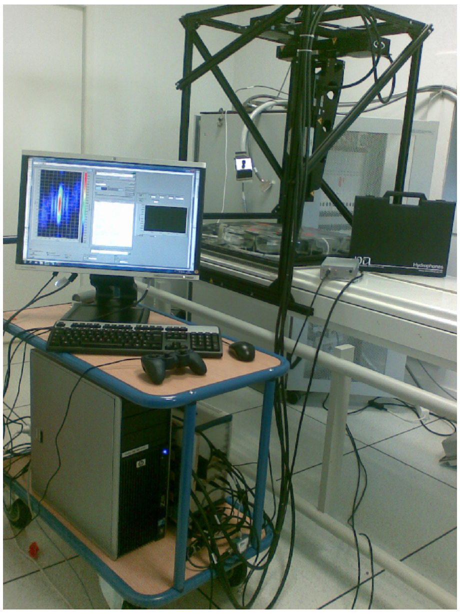
To compensate for manufacturing tolerances of the transducer modules, a phase calibration of the acoustic signal of each element at the focal point was performed in order to ensure optimal focusing in a water medium. The phase of each transducer element was adjustable in discrete steps of 3° and the required phase calibration and focal point shape measurements were performed in degassed water with a hydrophone system described in fthe subsequent manscript section.

The transducer was integrated in a MR compatible table top including a 3D mechanical positioning system and a dedicated MR breast coil. This Philips Sonalleve breast MR-HIFU platform was tested inside a Philips Achieva 1.5T scanner to identify phantom geometry and to compare heating efficiency of each refocusing method. Acoustic field measurements were acquired outside of the MRI room using a hydrophone set-up docked on top of this HIFU bed.

INSTALLATION OF A 3D HYDROPHONE SETUP WITH TAILORED SOFTWARE FOR PRECISE ACOUSTIC BEAM CHARACTERIZATION

Since the ultimate goal of the project is to develop a non-invasive method for beam refocussing, direct acoustic measurements are required to evaluate the resulting beam-quality. The focusing quality for each refocusing method was characterized with the hydrophone moving along 3 axes to acquire 3D acoustic field maps. This setup had two basic components: The mechanical platform and the acquisition electronics. The mechanical platform consists of a modular scaffolding of aluminum bars (25 mm structural elements sourced from Thor labs) which carry three linear stages M ILS-150PP (Newport, Irvine, California, USA) allowing the 3D displacement of the probe hydrophone. Motors were driven with stepper driver NI-MID-7604 (National Instruments, Austin, Texas, USA). The scaffolding is docked to the breast platform via a snap-on system to interleave acoustic and MRI measurements. Data acquisition was performed by the hydrophone with an integrated preamplifier of 20 dB and an additional fixed gain preamplifier PR-SA20D of 20 dB (lecoeurelectronique, Chuelles, France). Sampling was performed by a NI-PXIe-5122 AD-converter (National instruments, Austin, Texas, USA).

This set up was used in two different modes, either by switching on each transducer element sequentially for individual phase measurements to assess the aberration function, or by switching on all transducer elements simultaneously for the focal point characterization, as described below:



The scaffolding on the left is mounted on the experimental breast platform. The three linear stages allow a 3D sampling of the pressure distribution of the focal point area. The trolley on the right holds the acquisition electronics (motor drivers, amplifiers and ADC conversion) and the measurement computer. Displayed on the monitor is a pressure map of the focal point in a homogenous propagation medium.

Individual phase measurements

Since the accuracy of individual phase measurements at the focal point position strongly depends on the correct position of the hydrophone needle, a triangulation method was used to localize the geometric transducer center. For this, the sonication phantom was removed and replaced by degassed and demineralized water to provide a uniform celerity between each transducer channel and the hydrophone needle. When a single transducer channel is used as the signal source, the pulse delay measured by the hydrophone is proportional to the distance from the head of the needle to the center of this element. The known celerity of water multiplied by the delay provides a distance measurement D_n for each transducer element. The resulting 256 distances allow an accurate triangulation of the hydrophone head localization in 3D space relative to the geometric center of the transducer. After the focal point position was calibrated, the needle was driven to a parking position, which allowed to insert the acoustic phantom. Subsequently, the hydrophone was repositioned to the calibrated focal point position, exploiting the high repositioning precision of the linear stages.

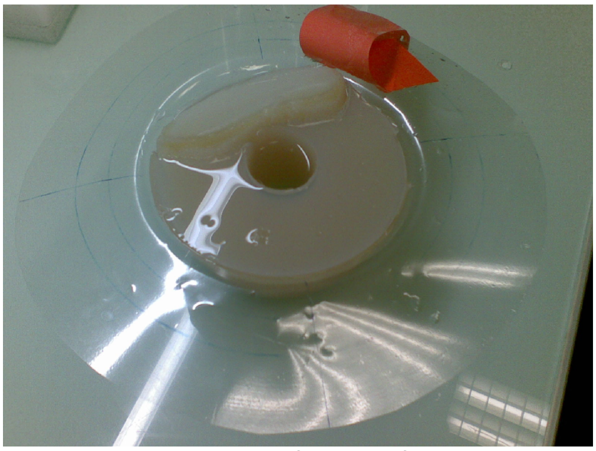
Once the hydrophone was in place, the relative dephasing between each transducer element at the focal point position was measured by activating sequentially each element for a brief pulse of 20 cycles and by comparing the relative phase difference of the measured hydrophone signal (transducer element #0 was chosen as the reference).

Characterization of the focal point

For the characterization of the form and amplitude of the focal point, all channels were periodically activated for a brief pulse of 20 cycles. Simultaneously, the linear stages performed a continuous sweep of the 3D volume around the focal point on a pre-programmed trajectory. The excitation pulses and the trajectory positions of the sweep where synchronized with the continuous acquisition of the acoustic signal with the hydrophone needle to result in a 3D map of the pressure distribution with a spatial resolution of 0.2x 0.2x 0.2 mm^3 and a field of view of 50x50x50 mm^3.

CONSTRUCTION OF A BREAST PHANTOM WITH SIMILAR ACOUSTIC PROPERTIES AND NMR CHARACTERISTICS THAN HUMAN BREAST TISSUE

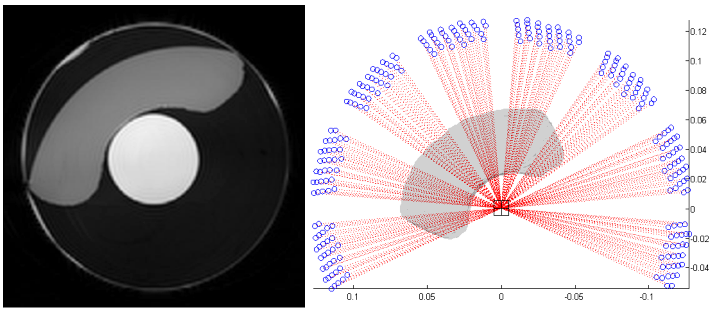
To mimic breast tissue heterogeneity, a two-component phantom consisting of a 3% agar-gel matrix (celerity 1485 m/s and attenuation 1.4 Np/m at 1.45 MHz) and embedded blocks of the polymer material (Model TTP1, ATS laboratories Inc., Bridgeport, CT, celerity 1528 m/s and attenuation 8 Np/m at 1.45 MHz) was made. The materials were selected in order to obtain celerities similar to in-vivo fat and glandular breast tissues [5]. The phantom contained a water-filled central conic recess allowing displacement of the hydrophone needle for three dimensional acoustic field mapping. In order to quantify the impact of the correction for HIFU ablations, the central aqueous conic part could be replaced with 3% agar + 3% silica gel matrix (celerity of 1447 m/s and attenuation of 4 Np/m at 1.45 MHz) in order to absorb the ultrasound wave at the focal point location, without modifications of the surrounding heterogeneous structure.



Breast phantom during the final manufacturing step: The polymer blocks are embedded in a gel-matrix, which is has been cast into a breast shaped mold. Note the well in the center of the phantom, which allow direct acoustic measurements.

DEVELOPMENT OF A 3D MRI SEQUENCE FOR TISSUE CHARACTERIZATION

The proposed approach used high-resolution MRI images to create a 3D description of the different tissue compartments within the HIFU beam path. The sequence used to obtain such contrast of different medium was a 3D TSE sequence (TR=1 s, TE=80 ms, TSE factor=30, α=90°) with a resolution 1×1×2 mm^3 and a FOV of 250×250×128 mm^3 acquired in 48 min, which was chosen to avoid geometric distortions. Alternatively, a rapid T_1 weighted gradient recalled echo sequence with a similar resolution and a total acquisition time of 12min was also evaluated.

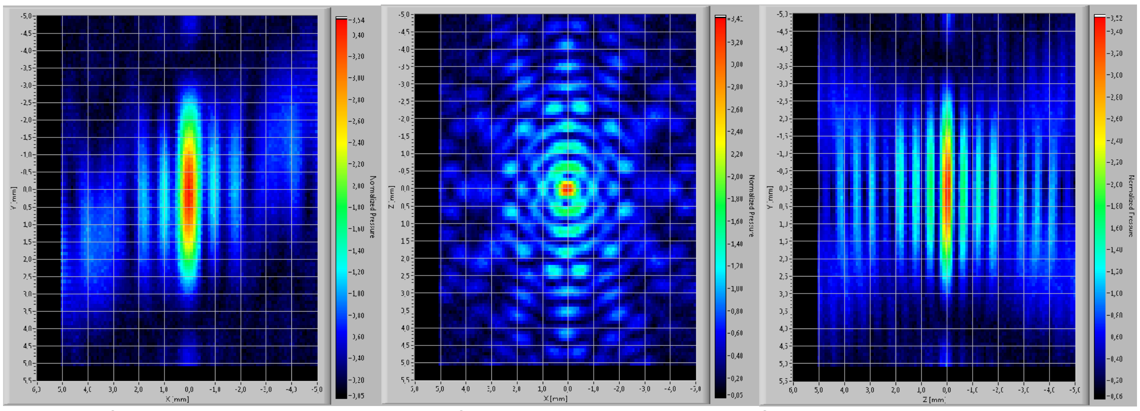


Coronal view of the 3D volumetric MRI (left) used to establish a 3D model of the tissue celerity, which is injected in a 3D simulation of the acoustic beam path (right).

The acoustic aberrator was segmented from the images with a semi-automatic tool written in IDL (ITT Visual Information Solutions, Boulder, Colorado, U.S.A) on a slice-by-slice basis. The surface of the obtained aberrator volume was subsequently tessellated in 3D space using a marching cubes algorithm similar to the algorithm described by Lorenson and Cline [6]. The resulting 3D surface was scaled from voxel to metric coordinates and the origin of the coordinate system was changed to the natural focus of the breast platform in transducer coordinates. Then, the surface objects were converted into the x3D format and imported into Matlab software (Mathworks, Natick, Massachusetts, U.S.A) for quantification of the corresponding phase correction and simulation of the resulting acoustic field.

DELIVERABLES Q2:

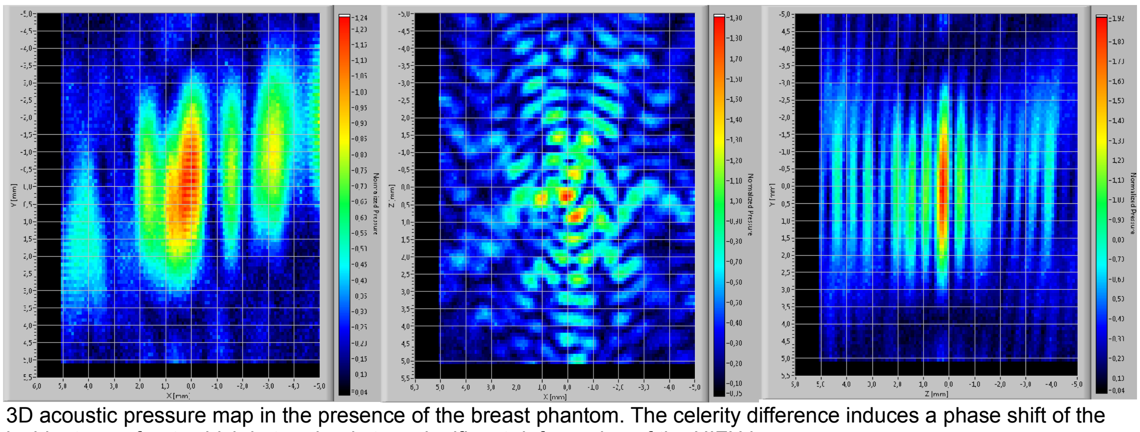
CHARACTERIZATION OF THE FOCAL POINT SHAPE IN A HOMOGENEOUS PROPAGATION MEDIUM



Example of the direct acoustic measurements of the pressure distribution in the focal point area: The three orthogonal planes show the principal focal point together with the numerous side lobes, which are a consequence of the transducer aperture.

The automatized 3D measurement of the pressure amplitude allows to characterize the focal point shape in less than 30min. The displayed example above shows the focal point of the wide-aperture system in degassed and demineralized water. The “dotted” ring of side lobes around the center maxima is a direct consequence of the geometric arrangement of the 256 transducer elements. The design of the measurement system allows to directly insert the breast phantom and to repeat the focal point characterization for direct comparison as shown below.

CHARACTERIZATION OF THE FOCAL POINT SHAPE IN THE INHOMOGENEOUS BREAST PHANTOM



3D acoustic pressure map in the presence of the breast phantom. The celerity difference induces a phase shift of the incident wavefront, which in turn leads to a significant defocussing of the HIFU beam.

The pressure distribution in a heterogeneous media in absence of any phase correction as shown above displays the significant loss of focus quality and peak pressure amplitude: The focal point is split into 2-4 lobes and the peak pressure is reduced to 69.6% of the initial value.
In the context of non-invasive thermotherapy this reduces the ablation efficiency and thus leads to a significantly prolonged duration of the intervention. Furthermore, a loss of focus quality increases the risk of undesired tissue damage in both the near-field, due to the increased required overall acoustic energy and in the areas adjacent to the focus.

DEVELOPMENT OF THE PHASE CORRECTION ALGORITHM FOR ACOUSTIC BEAM SHAPING BASED ON THE 3D MRI DATA

The 3D representation of the celerity distribution was used to calculate the resulting phase differences of the ultrasound waves at the focal point coming from each element as shown below. In order to achieve processing times compatible with a routine clinical preparation, straight-line propagation of the ultrasound from the center of each transducer element to the geometric center of the transducer was assumed for phase quantification. The intersections of each beam path line with each medium layer were processed to evaluate the acoustic propagation delay. For refocusing, the resulting phase φ^n of the acoustic wave coming from element n was derived from the linear combination (1) of the operating frequency f, the celerity of c^i of the medium i and the propagation wave distance d_n^i of the beam path line of the element n across this medium.

$$\phi^n = 2\pi \cdot f \cdot \sum_i \frac{d_n^i}{c^i} \qquad (1)$$

This processed noninvasive phase measurement was compared to the invasive reference phase measured channel per channel with the hydrophone needle placed at the center of the transducer.

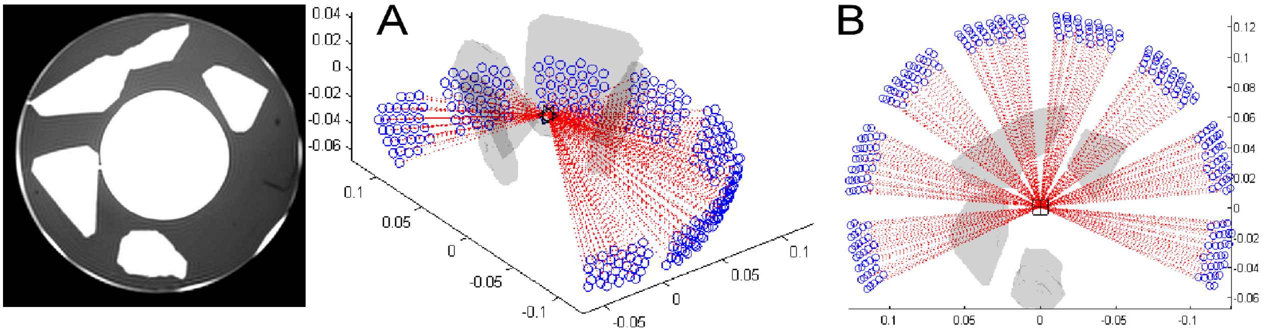
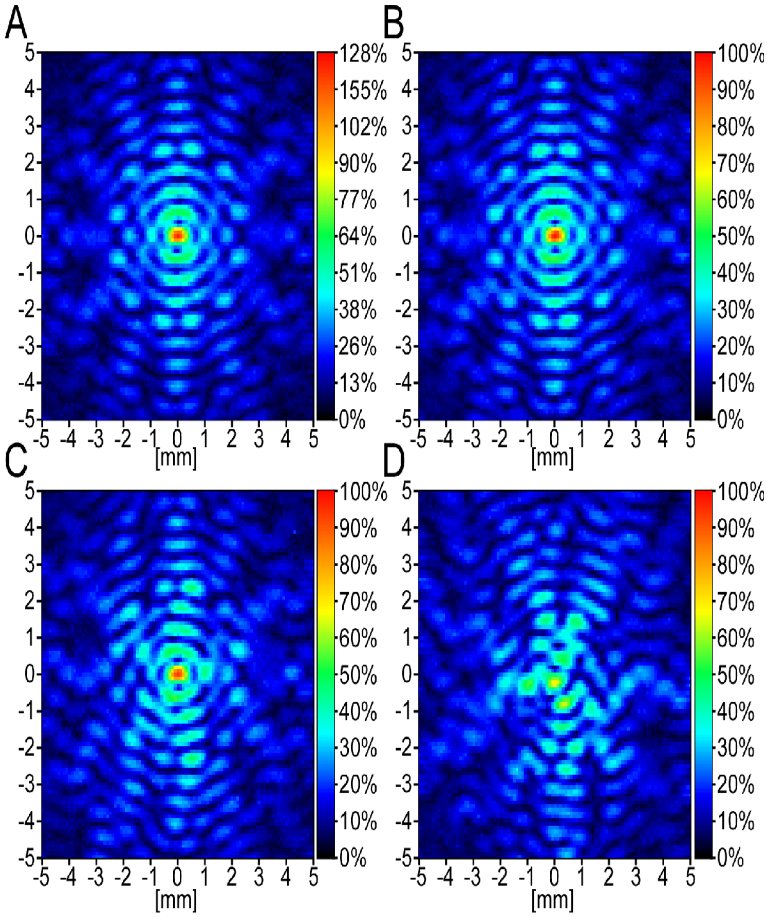


Figure 1:Coronal view of the 3D volumetric MRI which serves as a basis for a 3D model of the tissue celerity. The model is injected in a 3D simulation of the acoustic beam path (A,B). The resulting correction is used to optimize the focal point shape by compensating phase differences.

DELIVERABLES Q3 and Q4:

REFOCUSING (BEAM SHAPING) OF THE FOCAL POINT IN THE INHOMOGENEOUS BREAST PHANTOM BASED ON DIRECT ACOUSTIC MEASUREMENTS

REFOCUSING (BEAM SHAPING) OF THE FOCAL POINT IN THE INHOMOGENEOUS BREAST PHANTOM BASED ON MRI DATA AND THE ACOUSTIC MODELING



The measured normalized pressure distribution in the focal plane for a homogeneous propagation media (water (A)) for comparison and in a heterogeneous media (B, C, D). The result of figure (B) is obtained when a phase correction based on direct hydrophone measurements are used and serves as a reference. The pressure distribution shown in figure (C) is the result of a phase correction obtained from MRI-data, which is due to its non-invasive nature compatible compatible with clinical application scenarios. Note the good correspondence of both approaches (B,C). Finally, the pressure distribution obtained in absence of any phase correction shown in figure (D), dispays the loss in in amplitude and focus due to the aberrator.

Although both deliverables are currently work in progress, first experiments show some very encouraging results: The figure above presents the acoustic pressure distribution in a homogenous media (Fig 2A) and in a heterogeneous media (B,C,D). The reference experiment (Fig 2B) uses a phase correction based on direct phase measurements using a hydrophone at the location of the natural focus. In direct comparison the proposed phase correction based on MRI data (Fig 2C) shows a comparable focus quality. Finally, the pressure distribution in a heterogeneous media in absence of any phase correction (Fig 2D) displays the significant loss of focus quality and peak pressure amplitude: The focal point is split into two lobes and the peak pressure is reduced to 69.6% of the value obtained when using the invasive reference method for correction. In comparison, the non-invasive MRI based phase correction also allows to reestablish the original focal point shape and to regain 94.6% of the maximal achievable pressure amplitude.

Publications and conference contributions:

- Charles Mougenot, Julius Koskela, Matti Tillander, Max Köhler, Chrit Moonen and Mario Ries. **MRI based Heterogeneity Correction for Large Aperture HIFU Transducers**, *Proceedings of the International Society for Therapeutic Ultrasound (ISTU)* 2011, New York.
- Charles Mougenot, Julius Koskela, Matti Tillander, Max Köhler, Chrit Moonen and Mario Ries. **MRI based Heterogeneity Correction for Large Aperture HIFU Transducers**, *Proceedings of the International Society of Magnetic Resonance in Medicine (ISMRM)* 2011, Montreal.
- Charles Mougenot, Julius Koskela, Matti Tillander, Max Köhler, Chrit Moonen and Mario Ries. **High Intensity Focused Ultrasound with large aperture transducers: A MRI based focal point correction for tissue heterogeneity.** Submitted to the International *Journal of Hyperthermia in August 2011,* currently under review.

Concluding remarks:

Overall the project is well on track, with all of the deliverables of the first half of the project successfully completed. Since the first half of the project dealt predominantly with the required infrastructure, the stage is basically set for the actual experiments on the refocussing method. The grant anticipated to achieve refocussing with both direct acoustic phase measurements (deliverable Q3) and non-invasive phase estimations based on MRI data (deliverable Q4). As the report shows, both deliverables are currently work in progress and show already promising results, which lead to a first publication (currently under review).