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Thermo-therapie non invasive des organes abdominaux

Baudouin Denis de Senneville[1], Mario Ries[1], Bruno Quesson[1], Hervé Trillaud[2], Remi Berriet[3], Gérard Fleury[3], Chrit Moonen[1]

[1]Laboratory for Molecular and Functional Imaging: From Physiology to Therapy, CNRS/Université Bordeaux 2, FRE 3313, 146 rue Léo Saignat, F - 33076 Bordeaux

[2] Service de Radiologie, Hôpital Saint-André, CHU Bordeaux, 33000 Bordeaux, France

[3] Imasonic SAS - ZA rue des Savourots 70190 Voray/l'Ognon France.

Abstract: Non-invasive thermo-therapy of abdominal organs

Objective: Thermal therapies are rapidly gaining importance in oncology as an alternative to radio-therapy and surgery. The possibility to locally deposit thermal energy in a non-invasive way opens a path towards new therapeutic strategies with improved reliability and reduced associated trauma leading to improved efficacy, reduced hospitalisation and costs. Liver and kidney tumors represent a major health problem because not all patients are suitable for curative treatment with surgery. Currently, radio-frequency is the most used method for percutaneous ablation and the development of a completely non-invasive method based on MR guided high intensity focused ultrasound (HIFU) treatments is of particular interest, since the energy source is located outside the body. This project addressed technological challenges for the treatment of liver and kidney, related to their motion and their location within the thoracic cage.

Material and methods: This project proposed safe and non-invasive methods for MR-guided thermal ablation of malignant tumors of liver and kidney with HIFU. Real-time MRI was used to precisely control heat deposition with HIFU within the targeted pathological area despite the motion of these organs, in order to provide an effective treatment with a reduced duration and an increased level of safety for the patient. New technologies were studied for the development of matrix transducers able to generate high acoustic power.

Discussion: 3D Real-Time MRI guidance of a HIFU intervention as well as inter-costal firing were realized *in vivo* in pig liver during breathing under real-time MR thermometry over sustained periods of several minutes. The ability to generate acoustic power as high as up to five time the usual level was demonstrated in vitro thanks to the development of the new transducer technology proposed in this project.

Conclusion: A fully MR-integrated HIFU treatment platform dedicated to the treatment of cancer in mobile abdominal organs was developed.

Key words: Abdominal organs, Oncology, Real-time MRI, Thermo-therapy, Focused Ultrasound, HIFU transducers

Résumé: Thermo-therapie non invasive des organes abdominaux

Objectifs: Les thermo-thérapies gagnent rapidement en importance dans le domaine de l'oncologie comme alternative à la radio-thérapie et à la chirurgie. La possibilité de déposer localement l'énergie thermique de manière non-invasive ouvre une nouvelle voie vers des stratégies thérapeutiques plus fiables et moins agressives pour les patients, et permettront une réduction des temps et des coûts d'hospitalisation. Les tumeurs du foie et du rein représentent une problématique majeure, la chirurgie ne convenant pas à tous les patients. A l'heure actuelle, la méthode d'ablation par radio-fréquences est la plus utilisée. Le développement d'une méthode non-invasive basée sur les ultrasons focalisés guidés par IRM s'avère particulièrement intéressante, car la source d'énergie est extra-corporelle. Ce projet adresse des challenges technologiques pour le traitement du foie et du rein, associés à leur mouvement et à leur localisation en dessous de la cage thoracique.

Matériel et méthodes: Ce projet propose des méthodes non-invasives destinés au guidage d'une ablation thermique des tumeurs malignes du foie et du rein par ultrasons focalisés. L'IRM temps réel est utilisé pour contrôler le dépôt d'énergie avec prise en compte du mouvement de l'organe ciblé. Des nouvelles technologies de transducteurs matriciels capables de générer de forte puissance sont étudiées.

Discussion: Le guidage 3D en temps réel d'une intervention par ultrasons focalisés avec un tir inter-costal a été réalisé *in-vivo* sur le foie de cochons en respiration libre, en combinaison avec une thermométrie temps-réel pendant une durée de plusieurs minutes. La possibilité de générer des niveaux de puissance acoustique plus de 5 fois supérieurs aux niveaux habituels est démontrée in vitro grâce à la mise en oeuvre de la nouvelle technologie de transducteur proposée dans ce projet.

*Conclusion:*Une plateforme ultrasons focalisés intégrée à l'IRM et destinés au traitement du cancer sur les organes abdominaux a été développée.

Mots clés: Organes abdominaux, IRM temps réel, Thermo-thérapie, Ultrasons focalisés, Transducteurs HIFU

Texte

Introduction

Thermal therapies are rapidly gaining importance in oncology as an alternative to radio-therapy and surgery. The possibility to locally deposit thermal energy in a non-invasive way opens a path towards new therapeutic strategies with improved reliability and reduced associated trauma leading to improved efficacy, reduced hospitalisation and costs. Liver and kidney tumors represent a major health problem because not all patients are suitable for curative treatment with surgery. Currently, radio-frequency is the most used method for percutaneous ablation and the development of a completely non-invasive method based on MR guided high intensity focused ultrasound (HIFU) treatments is of particular interest, since the energy source is located outside the body. This project addressed technological challenges for the treatment of liver and kidney, related to their motion and their location within the thoracic cage.

1. MR-Temperature of mobile organs

Magnetic Resonance Imaging (MRI) systems was used for two tasks:

- Non invasive thermometer: MR-guidance offers the benefits of excellent target visualization and continuous temperature mapping using the proton resonance frequency (PRF) shift technique (the phase of the MR signal is directly proportional to the local PRF and thus the local temperature). Although the local temperature is a precise indicator for the energy deposition, it does not directly allow to estimate tissue damage and thus to determine the therapy endpoint. For this purpose, the concept of the equivalent thermal dose was introduced to reflect the biological effects of elevated temperatures on tissue. The tissue destruction is achieved when the equivalent thermal dose exceeds the lethal dose (which is taken as 43 °C during 240 minutes).
- Combined with advanced image-processing techniques, MR systems can be used for continuous target identification and tracking.

This implies increased temporal resolution of MR-imaging and effective removal of motion related artefacts in real time. For that purpose, the separate sub-workpackages were addressed :

1.1. Acceleration of MR-based thermometry imaging with help of parallel imaging methods
Although modern MRI scanners offer the possibility of acquisition acceleration using parallel imaging techniques, the TSENSE reconstruction has been investigated in the field of thermometry [1]. This method was of particular interest since it provides a dynamic update of calibration data sets, which is of particular interest for flexible array coils positioned around the abdomen.

1.2. Development of real-time adaptive temperature imaging
It is difficult in practice to acquire on-line 3D isotropic images because of the technical limitations, spatial and temporal resolution trade-offs, and low SNR associated with fast 3D acquisition sequences. One approach consists of aligning the normal vector of the slice orthogonal this motion vector and thus to contain the entire motion cycle within a 2D imaging slice. This, however, imposes severe constraints on the imaging geometry which might be for anatomical or diagnostic reasons unfavorable. It is also not possible to ensure that the target area remains during the entire motion cycle observable by a single static image slice. We developed an alternative approach which dynamically adapt the image location to the current target location. The slice position was continuously adjusted to the current target location using fast pencil beam navigator echoes. Subsequent real-time image processing on the image stream allows to obtain two types of information: First, the in-plane target position is located with sub-voxel precision. This, in combination with the retained slice tracking position may describe the complete target position in 3D space [2,3].

1.3. Real-time data processing and communications
The update rate and latency of a measured information are two crucial points when this information is used to drive the therapy. While the image sampling frequency of is purely limited by the MR-acquisition time, the latency is determined by the remaining acquisition time after echo-formation, the image processing time, the switching time of the HIFU-generator and the required data transport. Since commercially available MRI systems have several limitations for real-time adaptive imaging and fast real-time image transfer, two basic problems had to be addressed: 1) the MR-data transport from the MR-scanner to an external reconstructor; 2) the data reconstruction process. To ensure real-time thermo-therapy implementation with the high data flow of parallel imaging, an in-house optimized reconstruction pipeline has been developed. Our approach took benefit of a combined CPU/GPU architecture by offloading computational intensive calculations to the GPU and thus freeing the CPU for pipeline management and data preparation. All computationally intensive processing steps

can be dedicated graphics processing unit (GPU) which allows to complete all calculations on a typical image size of 128×128 voxels in about 15 ms [4].

1.4. In-plane 2D motion compensation strategies for real-time MR-thermometry on abdominal organs
MR-Thermometry for interventional guidance on abdominal organs is hampered by the constant displacement of the target due to the respiratory cycle and the associated thermometry artifacts. Ideally, a suitable MR-Thermometry method should for this role achieve a sub-second temporal resolution while maintaining a precision comparable to those achieved on static organs, while not introducing significant processing latencies. We proposed a computationally effective processing pipeline for 2D image registration coupled with a multi-baseline phase correction in conjunction with high frame-rate MRI as a possible solution [5,6,7,8,9,10]. The proposed MR-thermometry method was evaluated for five minutes at a frame-rate of 10 images/s in the liver and the kidney of 11 healthy volunteers and achieved a precision of less than 2 °C in 70 % of the pixels while delivering temperature and thermal dose maps on the fly.

2. HIFU ablation of mobile targets

2.1. HIFU motion compensation with target tracking
Due to the high perfusion rates of kidney and liver, sustained sonications which exceed the duration of the respiratory cycle are required to achieve a sufficiently high temperature elevation to induce necrosis. However, the constant displacement of the target due to the respiratory cycle render continuous ablations challenging, since dynamic repositioning of the focal point is required. In addition, the focal point position must be continuously re-adjusted to prevent undesired damage to adjacent tissue. We demonstrated that a HIFU system based on a phased-array US transducer and rapid electronic displacement of the focal point, in combination with advanced real-time processing of MR images with correction of motion artifacts in temperature mapping, allows a mobile target to be tracked in 3D during the heating procedure, and enables regional temperature control [2,3].

2.2. Modeling of the rib cage for intra-costal firing
Although HIFU is a promising method for the non-invasive treatment of liver tumors, the presence of ribs in the HIFU beam path remains problematic since it may lead to adverse effects (skin burns) by absorption and reflection of the incident beam at or near the bone surface. We developed a method for selection of the transducer elements to deactivate based on the relative location of the focal point and the ribs as identified from anatomical MR images was proposed. Regions of interest surrounding the ribs are projected onto the transducer surface by ray tracing from the focal point [11]. This approach demonstrated the feasibility to obtain a temperature at the focal point similar with and without deactivation of the transducer elements, indicative of the absence of heat efficacy loss (see Figure 1).

3. HIFU transducer development and systems integration aspects

Imasonic, partner of this project, developed a first Phased-Array transducer prototype integrating an advanced water cooling system for high power generation. MR-compatibility of materials and components were tested in the IMF laboratory. Practical evaluation of the transducer using a reduced number of elements (56) has demonstrated much improved thermal behaviour when operating at high power:

- Up to 20 W/cm² acoustic intensity was generated in vitro during 180 s, while the transducer heating was measured at a maximum of 20 °C.
- The maximum efficiency of the transducer was 80% (measured at nominal frequency), and was above 70% in a large frequency range.
- The compatibility with the current Philips MR-HIFU platform was demonstrated at the IMF laboratory, allowing the electrical matching of individual elements and driving in power.
- MR compatibility was enough to realise a correct thermometry at focus, but should be improved to give access to thermal measurements close to the transducer front face.

4. MRgHIFU: Preclinical and clinical testing

4.1. Preclinical evaluation of MRgHIFU ablation of the kidney and liver
The ability to perform MR-Thermometry and Dosimetry in-vivo during a real intervention was demonstrated on a pig kidney during an HIFU-heating experiment. A 3D Real-Time MRI guidance of a HIFU intervention was then realized on abdominal organs *in vivo* over sustained periods of several minutes. The method proposed for intra-costal firing was finally validated *in vivo* in pig liver during breathing under real-time MR thermometry [8,9,10,11].

4.2. Clinical studies
The HIFU platform provided by Philips for the clinical study has first been used outside the ANR project to include 20 patients in the field of a clinical research trial of uterine fibroids contributing to a certification from the European Community for treatment of uterine fibroids using this MRI-HIFU platform. The feasibility of the thermometry and organ tracking with this HIFU platform has been assessed. An extension of six months has been obtained until May 2011 for further testing of the cooled transducer and for initial clinical tests towards treatment of human kidney and liver.

Conclusion:

A fully MR-integrated HIFU treatment platform dedicated to the treatment of cancer in mobile abdominal organs was developed. 3D Real-Time MRI guidance of a HIFU intervention as well as inter-costal firing were realized *in vivo* in pig liver during breathing under real-time MR thermometry over sustained periods of several minutes.

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Figure legend

Figure 1. Comparison of temperature data near the ribs during HIFU sonications performed in pig liver *in vivo*, without and with deactivation of the transducer elements. The graphs show the temperature evolution in a single pixel located (a) near the rib and (b) in the cartilage (see white points for exact location in each insert). The red curves show the temperature evolution when all the HIFU elements are active and the black curves show the temperature evolution when 124 elements were deactivated. The HIFU sonication duration (20 s) is represented by the gray rectangles. The horizontal bars show the average values of temperature between 100 and 200 seconds. Images (c) and (d) are maps of the average temperature values (the color scale is indicated on the right) in each pixel between 100 and 200 s (vertical dashed blue lines in a and b).
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Figure
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