Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

In-vivo non-invasive motion tracking and correction in High Intensity Focused Ultrasound therapy

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Abstract— **A method for tracking locally the 3D motion of biological tissues is developed and applied to the correction of motion during High Intensity Focused Ultrasound (HIFU) therapy. The motion estimation technique is based on an accurate ultrasonic speckle tracking method. A pulse-echo sequence is performed for a subset of the transducers of a phased array. For each of these sub-apertures, the displacement is estimated by computing the 1D cross-correlation of the backscattered signals acquired at two consecutive times. The local 3D motion vector is then computed using a inversion algorithm. This technique is experimentally validated in vivo on anesthetized pigs. The 3D motion of liver tissues is tracked in real-time. The technique is combined with HIFU sequences and a real-time feedback correction of the HIFU beam is achieved by adjusting the delays of each channel. The sonications "locked on target" are interleaved with very motion estimation sequences.**

I. Introduction

Motion tracking techniques have been widely investigated in medical applications such as radiotherapy and imaging. Respiratory gating is a conventional technique for addressing the problem of breathing motion [1],[2]. External sensors (spirometer, strain gauge or infrared laser sensors fixed onto the patient's skin) are monitored during the treatment [3], and the therapeutic beam is switched off whenever the target is outside a predefined window. Most of the current commercial systems allow the operator to monitor the amplitude of displacement and not its direction. Therefore, although external sensors can be used to optimise the delivered dose and to reduce the effect of large motion, no feedback is introduced in the therapeutic or imaging system to correct the motion.

In this study, we present an novel ultrasound-based method for tracking the 3D motion of tissues in real-time. This technique is based on tracking temporal shifts in the backscattered RF signals (i.e. speckle) resulting from the displacements of the tissues. The main advantage of ultrasound-based methods is the high penetration rate of ultrasound in the human body and their real-time capabilities. Hence, the natural ultrasonic scatterers in biological tissue can be used as markers to track local motion of tissues located deep within organs. In other words, unlike other motion tracking techniques, the method that we propose works without any implanted markers.

Moreover, this method can be integrated easily in a High Intensity Focused Ultrasound (HIFU) multi-channel system. HIFU is a promising technique for non-invasive treatments of localized tumours in various organs, such as liver[4], prostate [5], kidney [6], brain [7] and breast [8]. A high power ultrasonic transducer is used to focus ultrasound in a small region and to generate a lesion (usually the lateral dimension is about 1 mm, and the axial dimension is about 7mm) through thermal and mechanical effects. Then, the treatment of large tumours is achieved by scanning mechanically or electronically the focus over the region of interest. However, accurate targeting in human abdominal organs is difficult to ensure due to motion. Abdominal organs can move as much as 10 mm over the breathing cycle with speeds of up to 10mm s^{-1} [9]. Therefore, the reliability and efficiency of treatment is greatly reduced by motion [10].

In this paper, a novel 3D motion tracking technique is integrated into an existing HIFU multi-channel system with real-time capability. In vivo feasibility is shown in the liver of anesthetized animals. Finally, another important innovation of this method consists in using the 3D position information as a feedback for the HIFU system: the transmit delays are modified instantaneously in order to electronically steer the high-power ultrasonic beam towards the corrected location.

II. Materials and Methods

A. 3D motion estimation

This method is based on estimating the local motion of tissues using ultrasonic transducers along at least three different directions. The transducers are used in pulse-echo mode : an ultrasonic pulse is focused by one transducer at a predetermined location inside of the tissue, and the backscattered ultrasound signal is received by the same transducer. The same process is repeated for the other transducers focusing at the same location.

The axial displacement is estimated for each transducer using two successive acquisitions. A classical speckle tracking

Manuscript received April 24, 2006. This work was supported in part by the Fondation de l'Avenir pour la Recherche Médicale Appliquée.

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algorithm is implemented [11]: a 1-D cross-correlation is performed on the two consecutives signals allowing an accurate estimation of the time-shift induced by the motion of tissue between the two acquisitions. Thus, one time-shift is estimated for each transducer, corresponding to the component of the 3D displacement vector $\vec{d}(d_x, d_y, d_z)$ along the sub-aperture beam axis. For transducer *i,* the time shift t_i is given by (where *c* is the sound velocity):

$$t_i = 2\frac{a_{ix}dx + a_{iy}dy + a_{iz}dz}{c} \quad (1)$$

Once the time-shifts estimated for each transducer, the set of linear equations given by eqn (1) is inverted in order to solve for the three components *dx*, *dy* and *dz* of the displacement vector. Of course, this set of equations would be completely determined if the estimation is made for at least three separate transducers. Although the estimation process would be faster in terms of insonification time, three transducers may not be optimal in terms of estimation robustness, and having more transducer would allow the estimation to be more stable. Indeed, if the displacement vector is normal to the beam axis of a sub-aperture, it induces a fast decorrelation of the speckle and the axial displacement becomes difficult to estimate accurately.

In order to avoid such a situation, it is possible to work with

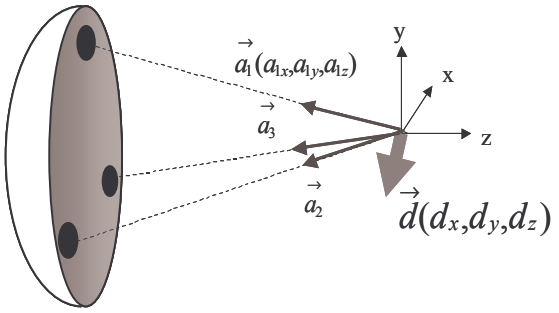

Fig. 1. Motion tracking setup with three transmitting-receiving transducers.

more than three transducers and to solve the over-determined set of linear equations by the least-square method. The set of linear equations is written in matrix form (see eqn (2)). In this formulation, a matrix *A* of size *N*x*3* is filled with the coefficients (a_{ij}), the j^{th} spatial component of the vector $\vec{a}_i(a_{ix},a_{iy},a_{iz})$. The vector *t* contains the *N* time-shifts, and *d* is the unknown displacement vector:

$$\begin{pmatrix} t \end{pmatrix} = \frac{2}{c}\begin{pmatrix} A \end{pmatrix}\cdot\begin{pmatrix} d \end{pmatrix} \quad (2)$$

The pseudo-inversion of the matrix *A* is computed using singular value decomposition ($A=U.W.V$ where *U* is a Nx3 orthogonal matrix, *W* a 3x3 diagonal matrix and *V* a 3x3 orthogonal matrix), and the least-squares solution vector *d* is given by:

$$\begin{pmatrix} d \end{pmatrix} = \frac{c}{2}\begin{pmatrix} V \end{pmatrix}\cdot\begin{pmatrix} diag(1/w_j) \end{pmatrix}\cdot\begin{pmatrix} U^T \end{pmatrix}\cdot\begin{pmatrix} t \end{pmatrix} \quad (3)$$

The displacement estimation process is summarized in Fig. 2. It should be noted that in practical applications, the singular value decomposition is computed once, so that the vector displacement is obtained with one matrix multiplication, a very simple and fast operation.

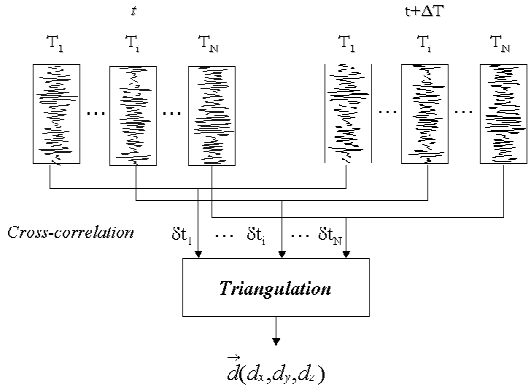

Fig. 2 3D vector displacement estimation process using N transducers or sub-apertures. At time *t*, *N* backscattered signals are recorded and stored in memory. At time $t+\Delta t$, *N* new signals are recorded and cross-correlated with the previous ones. *N* time-shifts are determined and used in a trangulation algorithm to compute the displacement vector.

B. High power ultrasound phased array

This technique can be used with a limited number of individual transducers (at least three) for motion tracking experiments or in combination with any kind of classical 2D ultrasonic array in order to couple imaging or therapeutic applications to the motion tracking technique. In this paper, we show the in-vivo feasibility of this technique using a high power 200 elements phased array [12]. The 200 high power piezocomposite transducers (8 mm diameter, 0.5 cm^2 active area, 900 kHz central frequency, Imasonic, Besançon, France) are mounted in a sealed spherically curved holder with a 12 cm radius of curvature. The transducers are connected to a 200-channels electronic driving system. Each electronic channel is individually programmable and possesses its own emission/reception electronic board. This phased array was optimized for electronic beamsteering in HIFU applications and therefore the focus can be moved up to 20 mm from the geometric focus by adjusting the delays of each channel. Figure 3 shows the 200 transducers distribution.

Taking advantage of the great versatility of the multi-element technology, four groups of transducers of about 25-

mm in diameter were designed on the phased array for the motion tracking technique. The sub-apertures were chosen in order to maximize the steering angles, and maximize the accuracy of the displacement estimation [4]. Figure 4 shows the four sub-apertures composed of seven transducers. In the receive mode, the sub-apertures could be also sized to any dimension. The receiving sub-apertures could be also of different size depending of the desired focusing quality. However, in our system the signals were collected on a computer using a serial ISA bus and the transmission time increases with the number of receiving transducers. As a consequence, the data transfer rate of our ISA bus limited the number of receive transducers. Though it is not a critical point at this time, these features could be implemented in hardware to diminish the time needed for the motion estimation. Finally, the transmitting subapertures were chosen as drawn in fig. 3, and the transducer located in the center of each subaperture was used in receive mode.

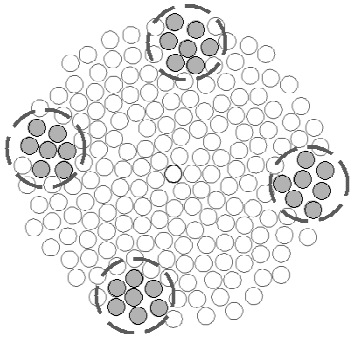

Fig. 3 Four subapertures designed on the phased array.

C. *Motion tracking/HIFU Sequences*

An initial pulse-echo sequence was performed on the four sub-apertures. The recorded signals were then digitised, recorded by the multi-channel electronics and transmitted to the computer. A second pulse-echo sequence was then performed, and based on the two consecutive RF signals, the cross-correlation algorithm estimates the time-shifts between the two acquisitions. By inversing equation (3) the 3D displacements vector was calculated and added to the initial position. The whole process could be repeated at a high frame rate, the minimal time between acquisition depending on the transmitting-receiving sequences (approximately 200 µs for each sub-aperture), the ISA bus transmission duration (about 3ms), and the displacement estimation duration (less than 1ms). Thus, the complete process was achieved in less than 5ms and could be repeated at a frame rate up to 200Hz.

However, such high frame rate was not necessary for normal physiological motions that have limited velocities (max. 10mm/s). Therefore, small HIFU sequences were interleaved between the motion tracking sequences in order to perform HIFU therapy at the same time. Moreover, based on the tissue displacement estimation, new phase delays were computed in order to steer the beam of the phased array and

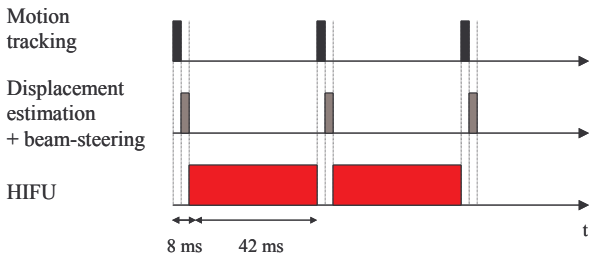

Fig.4 Motion tracking and HIFU Sequences for real-time motion tracking and correction.

allow the therapeutic beam to follow the motion of the tissue and to keep "locked on target". The phase delays were calculated and computed in approximately 3ms and small sequences of 42ms were used for the therapeutic beam. The sequences are shown in Fig 4. A duty cycle of about 86 % was achieved for the HIFU treatment.

D. *Animal preparation*

The experiments were part of a protocol approved by the animal experimental committee of the Institut Mutualiste Montsouris. Three female pigs were used for these experiments. The animals were anesthetized and maintained under ventilation during the experiment. The hair on the abdomen was removed using depilatory cream and the ultrasound phased array was placed on the chest using degassed ultrasound gel.

III. In vivo Experiments

Motion tracking experiments were conducted in vivo in order to demonstrate the ability of our technique to track in

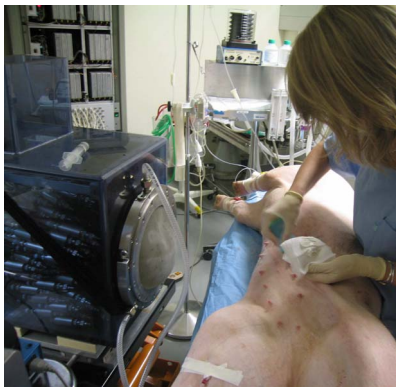

Fig. 5 In vivo experiments: on the left the ultrasound system with a latex bag filled with degassed water for coupling system. On the right the animal is prepared and ultrasound gel is applied over the chest.

vivo local motions of liver tissues. First, the liver was located using an imaging ultrasound scanner (vivid5, GE). Then, the phased array was placed in order to focus inside the determined location of the liver, at a depth of approximately

20mm from the liver surface. The motion tracking and the HIFU sequences were applied with total durations that varied between 30 and 120 seconds. Figure 6 shows the motion of the liver region which is inside the focus of our phased array. The three measurement directions corresponds approximately to the superior-inferior motions, the lateral motions and the posterior anterior motion. In these experiments, respiration induced motion was found to be mainly along the superior-inferior direction with amplitude that ranged between 2 and 6 mm depending on the animal and the region of the liver.

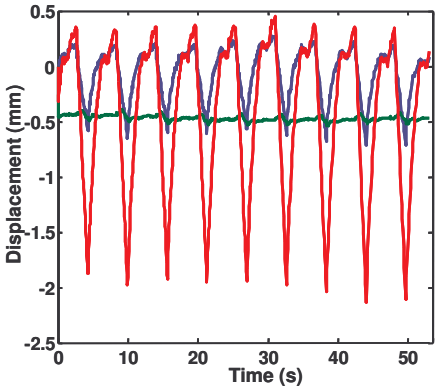

Fig.6. 3D Displacement of the liver non-invasively measured during the experiment. Red curve: superior-inferior motion. Blue curve: lateral motion. Green curve anterior-posterior motion.

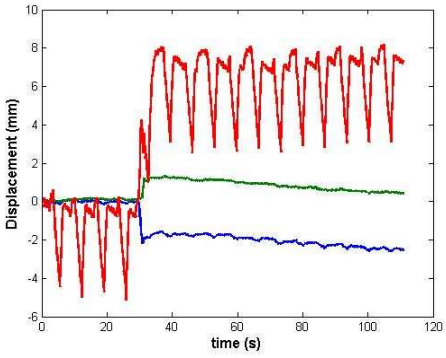

Fig.7. 3D Displacement of the liver non-invasively measured during the experiment. Red curve: superior-inferior motion. Blue curve: lateral motion. Green curve anterior-posterior motion.

Another important application of this technique is the detection of large accidental motions during the treatment. Indeed it is important for the safety of the treatment to ensure that the therapeutic beam will be turned off if such motions occur. In one experiment, the animal under anesthesia made suddenly a large movement during the treatment. Figure 7 shows that the motion tracking technique allowed the detection of a sudden motion in the three directions of approximately 10mm in amplitude.

IV. Conclusion

An ultrasound-based technique for real time 3D motion tracking and feedback correction in HIFU therapy was proposed and validated. This study demonstrates the ability of our motion tracking technique to measure the motion of the liver in animals under ventilation. Moreover, phase shift corrections were applied in real-time on each element of the HIFU array in order to steer electronically the beam and correct the tissue displacements. Interleaving fast 3D motion tracking sequences with longer heating sequences at a typical repetition rate of 10-50 Hz, allowed us to ensure a "locked on target" HIFU beam. Ongoing investigations deal with measurement of the effect of motion correction on HIFU treatments. Beyond the evident interest of motion correction for the improvement of HIFU targeting in abdominal organs, motion correction should lead to a important reduction of the treatment duration and total acoustic intensity deposit in the body. Moreover the motion tracking technique could be used for motion correction in 3D imaging (CT and MRI).

References

[1] Kubo H, Hill B. Respiration gated radiotherapy treatment : a technical study. Phys. Med. Biol. 1996, 41;1: 83-91.

[2] S S Vedam, P J Keall, V R Kini, H Mostafavi, H P Shukla and Mohan R "Acquiring a four dimensional computed tomography dataset using an external respiratory signal", *Phys. Med. Biol.* **48**, pp. 45-62, H. Poor, *An Introduction to Signal Detection and Estimation*. New York: Springer-Verlag, 1985, ch. 4.

[3] Shirato H, Shimizu S, Kunieda T *et al*. Physical aspects of a real-time tumor-tracking system for gated radiotherapy. Int. J. Radiation Oncology Biol. Phys., 2000; 48; 4: 1187-1195.

[4] Wang Z, Bai J, Li F *et al*. Study of a "biological focal region" of High-intensity focused ultrasound. Ultrasound Med Biol 2003;29;5: 749-754.

[5] Chapelon JY, Ribault M, Vernier F, Souchon R, Gelet A. Treatment of localised prostate cancer with transrectal high intensity focused ultrasound. Eur J Ultrasound 1999 ;9;1:31–38.

[6] Damianou C. In vitro and in vivo ablation of porcine renal tissues using high-intensity focused ultrasound. *Ultrasound Med. Biol.* 2003;29:1321-30.

[7] Vykhodtseva NI, Hynynen K, Damianou C. Pulse duration and peak intensity during focused ultrasound surgery: Theoretical and experimental effects in rabbit brain in vivo. Ultrasound Med Biol 1994;20;9: 987–1000.

[8] Wu F, Wang Z, Cao Y *et al.,* Changes in biologic characteristics of breast cancer treated with high-intensity focused ultrasound**,** *Ultrasound Med Biol.,* 29, 10, 2003, 1487-1492

[9] SC Davies, AL Hill, RB Holmes, M Halliwell, and PC Jackson "Ultrasound quantitation of respiratory organ motion in the upper abdomen." *Br J. Radiol.* **67**;pp. 1096-102, 1994.

[10] Wang H, Ebbini ES, O'Donnell M, Cain CA. Phase aberration correction and motion compensation for ultrasonic hyperthermia phased arrays: experimental results. IEEE Trans. Ultrason., Ferroelec., Freq. Contr. 1994;41;1:34-43

[11] M Tanter, J Bercoff, L Sandrin and M Fink "Ultrafast Compound imaging for 2-D motion vector estimation: application to transient elastography", *IEEE Trans.Ultrason. Ferroelec. Freq. Contr.* **49**,10 1363 – 1369, 2002.

[12] M Pernot, J-F Aubry, C Dorme, M Tanter and M Fink "200 Elements Fully Programmable Random Sparse Array for Brain Therapy: Simulations and First *Ex vivo* Experiments." *Proceeding of the ISTU*, Seattle, 2002