ESTIMATION OF MOUSE CONTRAST ECHOCARDIOGRAPHY SETUP WITH SECI

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Abstract: This work shows the use of SECI (Simulation of Echo Contrast Imaging). We present here results applied to mice cardiac imaging with contrast in the particular case of Contrast Pulse Sequence (CPS) imaging. Imaging mice is very different from imaging human because it is much smaller. In the case of mice echocardiography, transmit frequency must be higher than in human to preserve resolution. We study here transmit frequencies from 5 MHz to 13 MHz. Results show that at these frequencies, usual contrast imaging techniques focusing on the second harmonic cannot be used because of the probe bandwidth which filters out most of the higher harmonics.

Introduction

Myocardial contrast echocardiography (MCE) allows non-invasive assessment of myocardial perfusion. Small animal models are now extensively used in basic cardiology study. MCE in murine models requires the use of high-frequency probes usually from 8 MHz to 13 MHz. However, the behaviour of contrast agents has not been fully investigated with such frequencies.

We propose to investigate this application field with a simulator of echocontrast. The imaging modality used in this study: Contrast Pulse Sequences (CPS) is implemented on the Siemens machines. This modality is also pretty new and complex. So it is not so obvious for users of this imaging modality to foresee the influence settings have on the image.

Description of SECI

SECI (Simulation of Echo Contrast Imaging) has been developed to simulate contrast imaging with echography. It is a simulator that is able to perform any simulation of echocontrast imaging. SECI covers the full process of the echoscanner from transmit signal generation to beam forming and ultrasound wave propagation through the medium. Linear and stationary non-linear oscillations of bubbles are simulated, so, small amplitudes waves (Mechanical Index lower than 0.6) are handled. However SECI cannot simulate bubbles destruction. As it simulates contrast imaging, contrast specific imaging modalities, such as harmonic imaging, pulse inversion and CPS [1] is implemented.

Generation of the phantom: The phantom is generated according to user choices. The user sets the geometry of the phantom, sizes and zones with contrast, tissue or both. Within this geometry, the scatterers are placed according to desired concentration for each zone. A random generator uniformly distributes positions of scatterers (tissue and bubbles) within each zone. The amplitudes of tissue scatterers are gaussian distributed. The radius of the bubbles may follow any given probability distribution.

Ultrasound wave propagation is performed through Field II [2],[3]. Field II simulates the propagation of ultrasound waves in the far field of a linear medium. In the simulator, propagation is supposed to be linear. Moreover the phantom is in the far field (by using mathematical elements small enough in Field II). Field II gives the pressure wave at any point of the phantom. The pressure is computed at all positions of the scatterers.

The Mechanical Index (MI) is set by the user. So using equation (1) SECI calculates the pressure of ultrasound transmit wave.

$$p(\vec{r}_i, t) = MI\sqrt{f_{Tx}} \times \max_{neg}\left(h_t(\vec{r}_i, t)\right) \qquad (1)$$

where:

$\max_{neg}(.)$: takes the maximal value of negative oscillation, according to MI definition;
f_{Tx}: is the transmit frequency [Hz];
$p(r_i,t)$: is the pressure at location r_i [Pa];
MI: is the Mechanical Index;
$h_t(r_i,t)$: emitted spatial impulse response [$m.s^{-1}$].

Scatterers response: Scatterers fall into two classes, tissue and contrast agent. Tissue scatterers are modelled by diracs of different amplitudes while contrast agent has a non-linear behaviour. The model chosen is the non-linear differential equation proposed by Morgan [4]. It derives from a modified Herring equation (2).

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$$\rho_l R\frac{d^2R}{dt^2}+\frac{3}{2}\rho_l\left(\frac{dR}{dt}\right)^2 = \left(P_0+\frac{2\sigma}{R_0}\right)\left(\frac{R_0}{R}\right)^{3\gamma}\left(1-\frac{3\kappa}{c}\frac{dR}{dt}\right) - \frac{4\mu_l}{R}\frac{dR}{dt}-\frac{2\sigma}{R}\left(1-\frac{1}{c}\frac{dR}{dt}\right) - \frac{2\chi}{R}\left(\frac{R_0}{R}\right)^2\left(1-\frac{3}{c}\frac{dR}{dt}\right) - 12\mu_{sh}\varepsilon\frac{1}{R(R-\varepsilon)}\frac{dR}{dt} - \left(P_0+p(\vec{r}_i,t)\right) \quad (2)$$

where:

R	is the instant radius of the bubble [m];
ρ_l	is the density of the liquid [kg.m^{-3}];
σ	is the surface tension coefficient;
κ	is the polytropic gas exponent;
χ	is the shell stiffness [N.m];
ε	is the tickness of the shell [m];
μ_l	is the viscosity of the liquid [Pa.s];
$\mu_{sh}\,\varepsilon$	is the shell friction [N.m];
P_0	is the hydrostatic pressure [Pa].

As it can be seen, this model depends on many physical properties. The model describes the radius variation of the bubble given the driven pressure. Then the pressure due to these oscillations is calculated using the equation (from acoustic bubble from [5]):

$$p(R_0,t)=\sum_i\left(\frac{\rho_l\omega_i R_0}{1+\frac{\omega_i R_0}{c}}\cdot\left(\frac{\omega_i R_0}{c}+j\right)\cdot A_i\cdot e^{\omega_i t+\varphi_i}\right) \quad (3)$$

where:

c	is the speed of sound [m.s^{-1}];
$Ai,\omega i,\varphi i$	are the amplitudes, the pulsations and the phases of the Fourier transform of the radius speed respectively.

In this case the bubble is modelled as a rigid sphere since all the properties of the bubble have already been taken into account in equation (2).

Shooting line: Considering the phantom size, the desired number of shooting lines and the probe, the direction of each line is calculated. In SECI, any known probe can be used. By default a sectorial phased array probe is chosen. So images are as close as possible to cardiac images.

RF line: The pressure generated by every scatterer is then back propagated to the probe summed and transformed in electric signal by the transducer. The electric signal corresponding to the response of all the scatterers (i.e. the radio frequency (RF) line associated to the current shooting line) results from the former processing. It can be resumed by the equation:

$$S_{RF}(t)=\sum_i\frac{1}{c^2}\,e(t)*imp_{EA}(t)*h_t(\vec{r}_i,t)*a(\vec{r}_i,t)*H_{SC}(\vec{r}_i,t,p(\vec{r}_i,t))*a(\vec{r}_i,t)*h_r(\vec{r}_i,t)*imp_{EA}(t) \quad (4)$$

where:

$s_{RF}(t)$:	backscattered pressure for the scatterer i [Pa];
$e(t)$:	electrical excitation of the transducer [V];
$imp_{EA}(t)$:	electro-acoustical transducer impulse response [Pa.V^{-1}];
$h_t(r_i,t)$:	emitted spatial impulse response [m.s^{-1}];
$H_{sc}(r_i,t)$:	scattering function for the scatterer i, function of the pressure, if it is a buble;
$h_r(r_i,t)$:	received spatial impulse response [m.s^{-1}];
$a(r_i,t)$:	attenuation function;
* :	time convolution operator.

Hypothesis: here is a recapitulation of all the hypothesis used in SECI:

Acoustic Field and Modelisation:
- Linearity of the propagation
- Far field assumption
- First order Born-approximation

Agent Modelisation:
- Deterministic bubbles model
- Destruction and modification of the bubbles by the acoustic field are discarded
- Bubbles responses is non linear
- Normalization coefficient found by experiments

Phantom Modelisation:
- Statistical model of tissue
- Amplitude of tissue scatterers is random
- Propagation in tissue is linear (and deterministic).

The volume of inclusion can be used. It aims at reducing the number of scatterers that are excited by a given shoot of the probe. The computation of the response of the bubble to a driven pressure can be quite long. So computing irrelevant responses from bubble faraway for the shooting line axis is a time waste that must be avoided. For each shooting line the energy received by each point of a mesh is calculated. Then all the points that received less than – 6 dB of the maximum are supposed irrelevant considering this shooting line. The threshold of – 6 dB may be changed. But the bigger the volume of inclusion is, the longer computation time gets, especially with high bubble concentrations.

The CPS imaging modality

Contrast Pulse Sequence (CPS) is a new imaging modality [1], implemented on Siemens machines. In this section we summarise the principles of this method. CPS can be seen as a generalisation of pulse inversion

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and power modulation. Indeed, CPS uses several shootings. In this paper, sequences of four shots are used. Each of these four transmit shots is based on a reference pulse which is scaled by a scalar factor α_i. There are amplitude and phase changes. So for a scan direction there are four shootings, and thus, four RF lines. Those lines are then weighted, by coefficients β_i, and summed to give a final RF-CPS line:

$$CPS(t) = \sum_{1}^{4} \beta_i \left(\text{Echo}\left(\alpha_i s_{ref}(t)\right)\right) \qquad (5)$$

where:

s_{ref} is the reference signal on which are based all transmit pulses;

Echo(.) is the operator which gives the response of the medium to an ultrasound wave.

As for pulse inversion, where summing or subtracting the two RF lines for a given direction emphasises very different aspects of the response, the choice of the weighting is very important. Each set of α factors is denoted by a letter (A, B, etc) and the weighting coefficients β_i, by a number (1, 2, 3, etc) [1]. So a sequence is the association of both a letter and a number, for instance A1.

Sequences: The simulator should allow testing a lot of these combination and so determining which are the best candidates to be tested in-vivo. Testing is applied here to the particular case of the mice echocardiographic imaging. The different sequences used are presented in table 1.

Table 1: The sequences used in this work and their effects (i.e. which harmonics they emphases).

Name	α	β	Emphases
A1	0.5; 1; -1;-0.5	-8;-1;1;8	First harmonic
A2	0.5; 1; -1;-0.5	2;1;1;2	Second harmonic
A3	0.5; 1; -1;-0.5	-2;-1;1;2	Third harmonic
A4	0.5; 1; -1;-0.5	0;1;1;0	Second and forth harmonic (PI)

Simulations

The phantom is composed, in this work, of two parts, one with contrast agent and the second with tissue. The size of the phantom is set according to mice heart. Its size is 4x6 mm, and the tissue scatterers are set so there are several scatterers of tissue per wavelength square surface, there are 44 tissues scatterers per mm^3.

Contrast agent: the contrast agent simulated in these experiments is Sonovue (Bracco SA, Geneve, Switzerland). The concentration of contrast agent is 20 000 bubbles/ml. The shell stiffness and shell friction are respectively 1.1 N.m and 0.45×10^{-6} kg/s. The radius of bubbles fits the distribution of radius of the Sonovue [6].

Echoscanner: The probe used is a linear phased array, centered at 10 MHz and the MI used is 0.10, see bandpass of the probe figure 1.

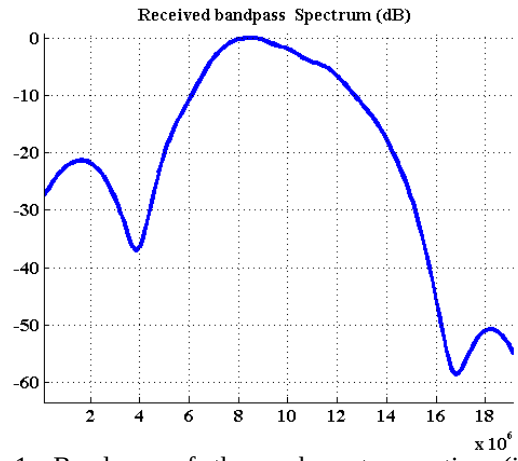

Figure 1: Bandpass of the probe, at reception (in frequency domain).

Parameter: In this work the only parameter which varies, is the transmit frequency. The transmit frequencies used are 5; 8; 10 and 13 MHz. For those frequencies the sequences A1, A2, A3 and A4 are compared.

Results

Method: For every one of these (the four sequences and the four frequencies), a CPS image was performed. As for the phantom these images can be decomposed into two parts, the tissue and the contrast agent. In this work, we chose to study the evolution of the contrast versus transmit frequencies for every sequence. The mean value of the envelope is calculated. So the value of contrast response is known for each sequence at every transmit frequency (5; 8; 10 and 13 MHz). The evolution over frequency for each sequence is shown on figure 2. The evolution of each sequence has been normalised because sequence should not be compared one to the other.

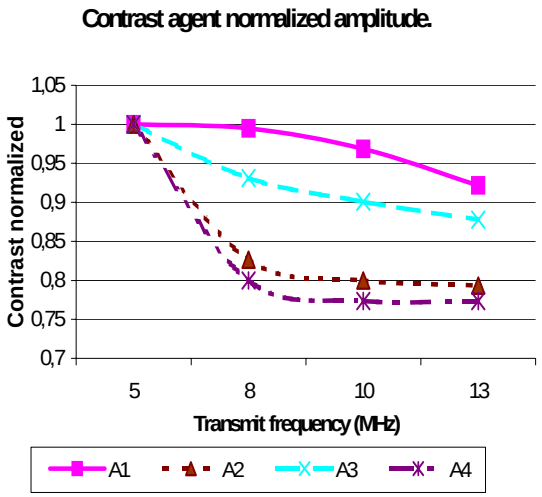

Figure 2: Evolution of the contrast intensity (mean of the envelope) versus transmit frequency. Each sequence is normalised by its maximum.

Interpretation: Figure 2 shows that when the frequency increases, the response of the contrast agent

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decreases. Indeed the higher the transmit frequency is, the more the probe filters the received signal which is to be taken into account. For instance, consider sequence A2 which focuses on the second harmonic of non-linear behaviour. If transmit frequency is 5 MHz, then it focuses on the frequencies around 10 MHz, which are in the bandpass of the probe. But if the transmit frequency is 8 MHz, the sequence focuses on frequencies around 16 MHz which are well outside the bandpass of the probe. So sequence A2 cancels most of the signal which is in the bandpass of the probe (because signal in the bandpass is not the second harmonic of the transmit frequency). Sequences A3 and A4 perform in the same way. Sequence A1 decreases much slower with the increase of the transmit frequency, because the fondamental frequency still lays in the bandpass of the probe (see figure 1), but getting attenuated.

Conclusion

In conclusion, in this work, performance of sequences A1, A2, A3 and A4 from CPS, has been mesured. In the application considered, mice myocardial contrast echocardiography, at high frequencies it has been shown that the bandwidth of the probe is a very important factor to take into account. Indeed, because transmit frequency is high, second harmonic (and higher ones) are filtered by the probe. As resolution is important for mice MCE, it can be concluded that, in this case sequence A1 and transmit frequency around 10 should be preferred.

In future, the simulator may be used to investigate different sequences to improve performance. The bandwidth effects are also to be studied in details to eventually propose improvements for this kind of exam.

References

[1] PHILLIPS P. (2001): 'Contrast pulse sequences (CPS): imaging nonlinear microbubbles', Proc of Ultrasonics Symposium, 2001, IEEE. Atlanta, USA, **2**, pp. 1739-1745

[2] JENSEN J., SVENDSEN N. (1992): 'Calculation of pressure fields from arbitrarily shaped, apodized, and excited ultrasound transducers', *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.,* **39**, pp. 262-267

[3] JENSEN J. (1996): 'Field: a program for simulating ultrasound systems', *Medical & Biological Engineering & Computing*, **34**, pp. 351-354

[4] MORGAN K. E., ALLEN J. S., DAYTON P. A., CHOMAS J. E., KLIBANOV A. L., and FERRARA K. W. (2000): 'Experimental and theoretical evaluation of microbubble behavior: effect of transmitted phase and bubble size', *IEEE. Trans. Ultrason. Ferroelect. Freq. Contr.*, **47**, pp. 1494-1509

[5] LEIGHTON T. G. (1996): 'The Acoustic Bubble', (Harcourt Publishers Ltd, a subsidiary of Harcourt International Ltd)

[6] GORCE J. M., ARDITI, M., and SCHNEIDER M. (2000): 'Influence of bubble size distribution on the echogenicity of ultrasound contrast agents: a study of SonoVue', *Invest. Radiol.* 661-71

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