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DUAL MODE REGISTRATION TO IMPROVE ESTIMATION OF PERFUSION PARAMETERS FOR ULTRASOUND IMAGE SEQUENCES

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ABSTRACT

The aim of this study is to present a new method for automatic motion compensation for ultrasound contrast imaging and to assess the impact on parametric perfusion imaging using linearized log-compressed data. Linear and non-linear ultrasound imaging are used for registration instead of one modality. The perfusion parameters estimated from the analysis of the time motion-compensated sequences of the contrast images show a great improvement in accuracy compared to the results obtained on uncompensated sequences and compensated sequences by linear images alone.

Index Terms— motion-compensation, ultrasound contrast imaging, parametric perfusion imaging.

1. INTRODUCTION

Contrast enhanced ultrasound (CEUS) imaging has been developed in order to visualize the micro-circulation in tissue [1] and to assess the perfusion measurements (the amount of blood that flows through a volume of tissue). Ultrasound contrast agents (UCA) are used in CEUS and are made as solutions of gas micro-bubbles in a fluid that can be administered intravenously to a patient to increase the scattering from blood. In addition to enhancing the sensitivity of ultrasound to blood flow, the micro-bubble contrast agents show a great potential for quantitative perfusion imaging [2]. Tissue perfusion is an essential indicator in clinical assessment of a wide range of clinical conditions such as heart diseases and cancer [2]. The evaluation of the quantitative parameters are needed to monitor changes in tumor micro-vascular blood flow.

There are several techniques for micro-bubble injection. With a bolus injection technique, the curves of image intensity are expressed as a function of time (time-intensity curves) for the quantification of blood flow in a region of interest (ROI) selected by an operator on one image. The time-intensity curve can be fitted with a mathematical model derived from the indicator-dilution theory [3] and defined by a set of parameters [4]. This mathematical approach leads to the analytical determination of important perfusion parameters [5] like peak intensity (PI), mean transit time (MTT), the area under the time-intensity curve (AUC).

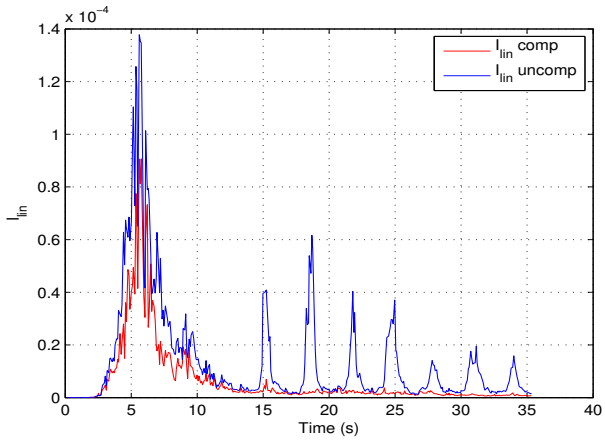


Fig. 1. Time-intensity curves with/without motion compensation.

One of the main problems in the estimation of perfusion quantification parameters is the motion present in the image sequence caused by internal organ or probe movements. ROI's selected by an operator don't strictly track the same zone throughout the sequence. To enhance the quality of the estimated perfusion parameters we need to compensate for this motion by image registration. The latter is obtained by performing a geometrical transformation between a reference image and moving images (images to be spatially aligned with respect to the reference image). Figure 1 shows an example of time-intensity curve with/without motion compensation. The application of the motion compensation reduces the variation of the intensity. A large number of methods for image registration in traditional ultrasound imaging are described in the literature [6]. But, a few range of registration methods are available for CEUS. The registration of contrast ultrasound images is a quite difficult task due to low signal-noise ratio, speckle and non-uniformity of tissue contrast uptake [7]. The best example of the application to CEUS acquisitions proposed in literature is given by Rognin and al. [8, 9]. They present a new approach for automatic motion

compensation based on the use of multiple mask method and predictive motion model [9]. Their approach is validated on parametric perfusion imaging and it improves the accuracy of the parameter estimates compared to the results obtained by original image sequence.

With certain imaging systems, linear images corresponding to tissue responses are acquired simultaneously with non-linear images detecting only the micro-bubbles flowing through the tissue. Such a system would allow the clinician to view the contrast agent signals separately from the tissue signals. The registration of the contrast images is usually achieved by alignment of linear images [10] obtained at different times during the passage of a contrast agent. Our first objective is to exploit two channels input data for registration: linear and non-linear sequences to improve motion compensation (and, thus perfusion quantification). The second is how we are going to combine the two channels together to give the best results. The final objective is to investigate if the motion compensation based on the two modalities provides better results than that based on linear images alone. In fact, the non-linear response of micro-bubbles reveals important details (micro-vasculature structures) which are not detected by the linear imaging and these details are complementary for image registration.

In this paper, we present a new approach called dual-mode for automatic motion compensation using: linear and non-linear imaging to improve the quality of the estimated perfusion parameters. Section 2 introduces the proposed registration method and the technical choices related to this method to help understand the added value of the dual-mode registration strategy. While section 3 presents the validation and the results obtained by our approach, Whereas section 4 discusses some general improvement and the perspective.

2. MATERIALS AND METHOD

2.1. Image Sequence Acquisition

Five hepatic CEUS sequences were acquired for patients with focal liver lesions. The contrast agent used was SonoVue (Bracco Spa, Milan, Italy) injected intravenously as bolus. When the contrast agent was administrated, contrast ultrasound sequence were acquired during 35 s to 50 s corresponding to 340 to 480 images. The image acquisition is obtained at a low mechanical index of 0.15 with a curved phased-array transducer 4C1-S connected to a Sequoia 512 ultrasound scanner (Acuson). Dual images in conventional (linear) and cadence CPS (Cadence Contrast Pulse Sequencing, Siemens-Acuson) were used for the acquisition and for the registration.

2.2. Registration strategy

Image registration determines the optimal geometrical transformation of moving images I_M, with respect to a reference image I_F using a similarity metric. From a mathematical point of view, there is an optimization problem in which the cost function $\mathcal{C}$ (similarity measure) is minimised via the transformation T_μ where μ is the vector of transformation parameters [6]

$$\widehat{T}_\mu = arg\min_{T_\mu} \mathcal{C}(T_\mu; I_F, I_M) \quad (1)$$

In this study, we used rigid transformation: two translations: vertical and horizontal (t_x, t_y) and one rotation θ_z in rad. Then μ is given by (θ_z, t_x, t_y). In the literature many choices have been proposed for the cost function $\mathcal{C}$. The commonly used intensity-based cost functions are the sum of squared differences (SSD), normalized correlation coefficient, mutual information (MI) [11] and normalized mutual information (NMI) [12]. The NMI is used in this study because it was found to be the most robust similarity criterion in the presence of changes in contrast [13]. We combine the two modalities together linear and non-linear to make the registration. Then, the total cost function is the sum of two cost functions $\mathcal{C}^l$ and $\mathcal{C}^n$. Each one depends on the type of the system imaging: linear/non-linear.

There are many strategies for the selection of the reference image in the registration of the contrast sequence. The first possibility is based on floating reference images: the second image is aligned with the first image; the third image is aligned with the second image etc. This is incremental registration [14, 15]. This method is not well adapted to linear images due to an accumulation of misalignments introduced by the incremental registration. The second possibility is to set only one reference image and the other images are aligned with respect to this fixed image. This method is called non-incremental registration [15]. It is not convenient for non-linear images because of the constantly-evolving properties of the contrast images.

The underlying principle of our approach is to use respectively the incremental and the non-incremental registration for non-linear and linear images [16]. With this manner of combination, we can avoid the problems of misalignments mentioned before. We note all the reference images by $I_F = (I_0^l, I_k^{n'})$ where I_0^l is the reference linear image and is fixed during the registration process and $I_k^{n'}$ are the floating reference non-linear images acquired at time t_k, and change during the process. The moving images are $I_M = (I_{k+1}^l, I_{k+1}^n)$ where I_{k+1}^l are the moving linear images acquired at t_{k+1} and I_{k+1}^n are the moving non-linear images. Then, the cost function is defined as:

$$\begin{aligned} \mathcal{C}(T_{\mu_{k+1}}; I_F, I_M) &= \alpha\, \mathcal{C}^l(T_{\mu_{k+1}}; I_0^l, I_{k+1}^l) \\ &+ (1-\alpha)\, \mathcal{C}^n(T_{\mu_{k+1}}; I_k^{n'}, I_{k+1}^n) \end{aligned}$$

α is the weight parameter, belonging to [0, 1] and chosen to be equal to 0.5. $T_{\mu_{k+1}}$ is the transformation to apply on the moving images acquired at t_{k+1}. To avoid the accumulation

of misalignment errors in the incremental registration for non-linear images, the floating reference non-linear images must be aligned using the last transformation.

$$I_k^{n'} = I_k^n(T_{\mu_k}) \tag{2}$$

A block diagram of the registration is shown in figure 2. Once the similarity measure has been defined the next task consists of finding the parameters that optimize the designed cost function usually by means of an iterative optimization method embedded in multiresolution optimization [6]. The experi-

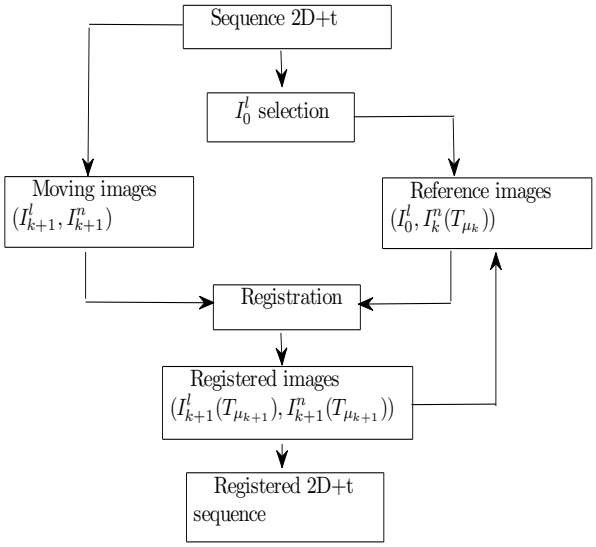


Fig. 2. Block diagram of the registration method

mental results in [17] indicate that an adaptive stochastic gradient descent method is a good choice for many applications. We used this technique to obtain the optimal transformation parameter vector $\widehat{\mu}$.

3. REGISTRATION EVALUATION

Several approaches may be considered for the validation of the image registration. The qualitative evaluation is a method based on visual inspection. This method is subjective and not accurate. Another method is the comparison with manual registration which needs a lot of time to accomplish the manual registration by the expert. Our approach consists of using a quantitative validation based on parametric imaging of the quality of fit (QOF) index [9]. The latter is then used to evaluate the quality of the registration and to compare our approach with the traditional method based on linear images alone.

3.1. Time-intensity model

The bolus kinetics analysis implies curve-fitting of the data which is a function of time. Ideally, a raw radio frequency (RF) echo-signal should be used for analysis. In our case we don't have these (RF) data and we only have log-compressed data in the form of DICOM files. A proper linearization is applied to reverse the log-compression before curve-fitting and analysis. A region of interest (ROI) is chosen inside the tumor in all acquired image sequences. Then, time-intensity curve is calculated by computing the average intensity of all pixel values in the ROI for the sequence. After, the curve is fitted using a parametric bolus model function $I_f(t)$ defined as:

$$I_f(t) = I_0 + \frac{AUC}{\sqrt{2\pi}\sigma(t-t_0)} e^{-\frac{(\ln(t-t_0)-\mu)^2}{2\sigma^2}} \tag{3}$$

which is the lognormal function and is chosen to fit time-intensity curve. AUC is the area under the curve, μ and σ are the mean and standard deviation of the normal distribution of the logarithm of the independent variable t, t_0 is the bolus arrival time, and I_0 is the baseline intensity offset. The figure 3 show time-intensity curve with motion compensation fitted with lognormal model.

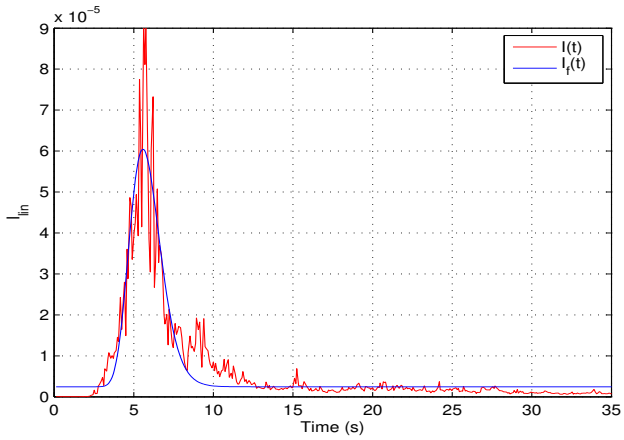


Fig. 3. Time intensity curve with motion compensation, $I(t)$ with its corresponding fitted curve $I_f(t)$

3.2. Parametric imaging

A parametric image is a spatial distribution of any perfusion parameter and is calculated from the analysis of time sequence of contrast images. We choose the quality of fit (QOF) [9] as a perfusion parameter. When the QOF is too low the related perfusion parameter can not be considered as reliable [9]. With motion compensation, the QOF should be improved. The QOF measures the difference between the time intensity curves $I(t)$ and its corresponding fitted signal

$I_f(t)$. It is given as:

$$QOF = 100\left(1 - \frac{SSR}{SST}\right)$$

Where SST is the sum of squares of differences

$$SSR = \sum_{t=1}^{N} \left(I(t) - I_f(t)\right)^2$$

where N is the number of samples, t is the sample index and SST is the sum of squared differences about the mean.

$$SST = \sum_{t=1}^{N} \left(I(t) - \overline{I}_f\right)^2$$

where $\overline{I}_f$ is the mean of $I_f(t)$.

3.3. Quantitative evaluation

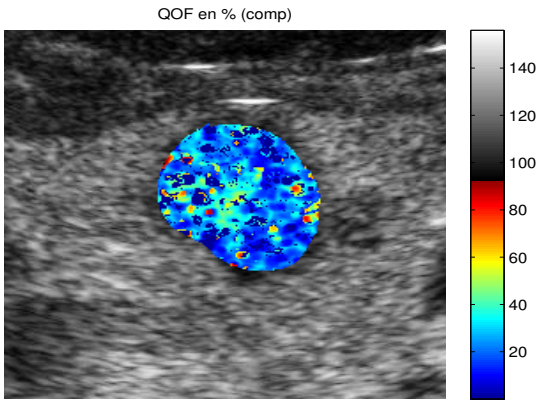
Table 1 shows the mean QOF for compensated sequences with: dual-mode and linear-mode registration method, and for uncompensated sequences. The linear-mode registration is based only on the linear images and uses the non-incremental registration method.

Patient	Comp. (%) Dual-mode	Comp. (%) Linear-mode	Uncomp. (%)
1	87	86	42
2	70	58	50
3	67	65	37
4	87	75	64
5	69	53	17

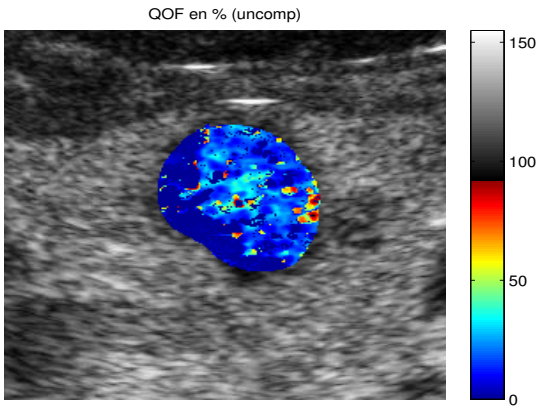
Table 1. Values of QOF for compensated and uncompensated sequences calculated for all the patients.

The mean QOF calculated for 5 patients increase strongly with our registration method comparing to uncompensated sequences and are higher than the values given by the linear-mode method. The QOF index differences between dual mode and linear mode vary from 1 % to 16 %. In the case of patient 1 and 3, the QOF index for dual-mode are close to the linear-mode. Therefore, the non-linear imaging is not able to add additional information to the linear imaging. But for the rest of patients, the difference is very large. This is explained by the fact that the use of both modalities improve the registration better than the use of one modality.

With such results we conclude a significant improvement in the assessment of perfusion. Figure 4.(a) and (b) show parametric images of QOF for compensated and uncompensated sequence respectively, calculated for patient 5 in the ROI. The red color in the parametric image is equivalent to a maximum of QOF in the image and the blue color represent a small value of QOF. The maximum of QOF is found in compensated sequence.



(a)



(b)

Fig. 4. (a) and (b) Parametric images of QOF computed for patient 5 on the compensated sequence with dual-mode registration and the uncompensated sequence, respectively.

4. CONCLUSION AND DISCUSSION

The proposed automatic registration method is based on the dual-mode: linear and non-linear imaging. Non-incremental registration is used for linear imaging and incremental registration for non-linear imaging. The dual-mode registration method performs a rigid transformation with normalized mutual information for similarity criterion. In the study, two cost functions are used. The first one is for linear imaging and the second is for non-linear imaging. Our technique used adaptive stochastic gradient descent method for the research of the optimal transformation parameters. The quality of fit index is used to evaluate the quality of the registration. It shows the ability of our compensation method to improve the accuracy of the perfusion estimation parameters. Further possible improvements may be explored. Firstly, the influence of the parameter α, tuning the weight of the linear/non-linear terms

(chosen equal to 0.5 in this study) could be investigated. Secondly, comparison with manual registration would be an ultimate validation of our method.

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5. REFERENCES

[1] D. Cosgrove, "Ultrasound contrast agents: An overview," *Eur. J. Radiol.*, vol. 60, pp. 324–330, Dec 2006.

[2] M. Xing Tang, J. Martial Mari, P. N.T. Wells, and R. J. Eckersley, "Attenuation correction in ultrasound contrast agent imaging: elementary theory and preliminary experimental evaluation," *Ultra. in Med. and Biol.*, vol. 34, no. 12, pp. 1998–2008, 2008.

[3] C. Strouthos, M. Lampaskis, V. Sboros, A. McNeilly, and M. Averkiou, "Indicator dilution models for the quantification of microvascular blood flow with bolus administration of ultrasound contrast agents," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 57, pp. 1296–1310, 2010.

[4] N. Lassau, L. Chami, B. Benatsou, P. Peronneau, and A. Roche, "Dynamic contrast enhanced ultrasonography (dce-us) with quantification of tumor perfusion: a new diagnostic tool to evaluate the early effects of antiangiogenic treatment," *Eur. Radiol.*, vol. 17, pp. 89–98, 2007.

[5] T. P. Gauthier, M. A. Averkiou, and E. L.S. Leen, "Perfusion quantification using dynamic contrast-enhanced ultrasound: The impact of dynamic range and gain on time-intensity curves," *Ultrasonics*, vol. 51, pp. 102–106, 2011.

[6] S. Klein, M. Staring, K. Murphy, M. A. Viergever, and J. P. W. Pluim, "elastix: A toolbox for intensity-based medical image registration," *IEEE Trans. on Medical Imaging*, vol. 29, no. 1, pp. 196–205, 2010.

[7] S. Mule, N. Kachenoura1, O. Lucidarme, A. De Oliveira, C. Pellot-Barakat, A. Herment, and F. Frouin, "An automatic respiratory gating method for the improvement of microcirculation evaluation: application to contrast-enhanced ultrasound studies of focal liver lesions," *Phys. Med. Biol.*, vol. 56, pp. 5153–5165, 2011.

[8] N. Rognin, M. Arditi, T. Messager, J.P. Thiran, and R. Campos, "An image registration method and apparatus for medical imaging based on multiple masks," *Patent Application Publication*, , no. US2008/0049994A1, 2008.

[9] N. Rognin, R. Campos, J. P. Thiran, T. Messager, A. Broillet, P. Frinking, L. Mercier, and M. Arditi, "A new approach for automatic motion compensation for improved estimation of perfusion quantification parameters in ultrasound imaging," *in Proc. 8th French Conf. Acoustics*, pp. 61–65, 2006.

[10] J. Zhang, M. Ding, M. Yuchi, and X. Zhang, "Respiratory motion correction in free-breathing ultrasound image sequence for quantification of hepatic perfusion," *Medical Physics*, vol. 38, no. 8, pp. 4737–4748, 2011.

[11] R. Kolar, R. Jirik, V. Harabis, K. Nylund, and O.H. Gilja, "Registration of ultrasound contrast images for perfusion analysis," *IUS*, pp. 1251–1254, 2009.

[12] T. Rohlfing, C. R. Jr. Maurer, D. A. Bluemke, and M. A. Jacobs, "Volume-preserving nonrigid registration of mr breast images using free-form deformation with an incompressibility constraint," *IEEE Trans. Med. Imag.*, vol. 22, no. 6, pp. 730–741, 2003.

[13] R. Shekhar and V. Zagrodsky, "Mutual information-based rigid and non-rigid registration of ultrasound volumes," *IEEE Trans. Med. Imaging*, vol. 21, no. 1, pp. 9–22, 2002.

[14] V. Harabis, R. Kolar, and R. Jirik, "Registration of ultrasound image for sequences for perfusion analysis," *EUSIPCO 2011, Barcelona, Spain, August 29 September 2*, 2011.

[15] E. J. Harris, N. R. Miller, J. C. Banber, J. R. N. Symonds-Taylor, and P. M. Evans, "Speckle tracking in a phantom and feature-based tracking in liver in the presence of respiratory motion using 4d ultrasound," *Phys. Med. Biol.*, vol. 55, pp. 3363–3380, 2010.

[16] N. Bouhlel, A. Coron, O. Lucidarme, and L. Bridal, "A new registration method to improve estimation of perfusion quantification parameters," *Journees Thematiques GDR :Imageries in vivo (IMAGIV2011), Des nouveaux concepts en imagerie a l'application clinique*, 2011.

[17] S. Klein, M. Staring, and J. P. W. Pluim, "Evaluation of optimization methods for nonrigid medical image registration using mutual information and b-splines," *IEEE Trans. Image Process.*, vol. 16, no. 12, pp. 2879–2890, 2007.