# REGISTRATION OF CONTRAST-ENHANCED ULTRASOUND SEQUENCES

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**Abstract**: The registration of contrast-enhanced ultrasound (CEUS) image sequences is necessary for correct perfusion analysis. Methods developed for CEUS images have to overcome the low signal to noise ratio, speckle noise and pixel intensity changes given by the application of ultrasound contrast agents. A method presented in this paper utilizes intensity-based algorithm.

**Keywords**: Contrast-enhanced ultrasound image, image registration

## 1. INTRODUCTION

It has been proposed and developed many methods for image registration. However, only few methods are designed for contrast-enhanced ultrasound (CEUS) image sequences, for example [1, 2]. The registration of ultrasound images is a difficult task due to the low signal to noise ratio (SNR) and due to the presence of speckles. Furthermore, in CEUS sequences, the ultrasound contrast agent (UCA) induces the large change of pixel intensities after injection.

During acquisition, a tissue moves in three directions ($x$, $y$, $z$). Consequently, 2D image sequences record a motion in the direction of axis $x$ and $y$. Motions in z direction therefore cause out-of-plane artifacts, which cannot be eliminated. Thus, the registration of 2D CEUS image sequences encounters the several main issues: low SNR, speckle noise, large changes in pixel intensities and motion z direction.

## 2. DATA

The here-presented registration method is proposed for the purpose of the perfusion analysis of a tumor in specific 2D image sequences (scanning one slice in time). A tested image sequence consists of 134 images. In figure 1, the 3 images of the tested sequence are illustrated. The first is acquired before UCA injection, the second is after UCA injection during contrast-filling stage and the third is after contrast-filling stage. Images contain a tumor tissue as well as other tissues such as skin. The interest area of the perfusion analysis is only the tumor tissue, so the registration is only focused on this tumor area (figure 2 – black ellipse). The success of the registration method is evaluated for the area outlined by the white rectangle in figure 2.

The image sequence was acquired using the Vevo® 2100 System. Untargeted Vevo MicroMarker contrast agent was used in an experiment.

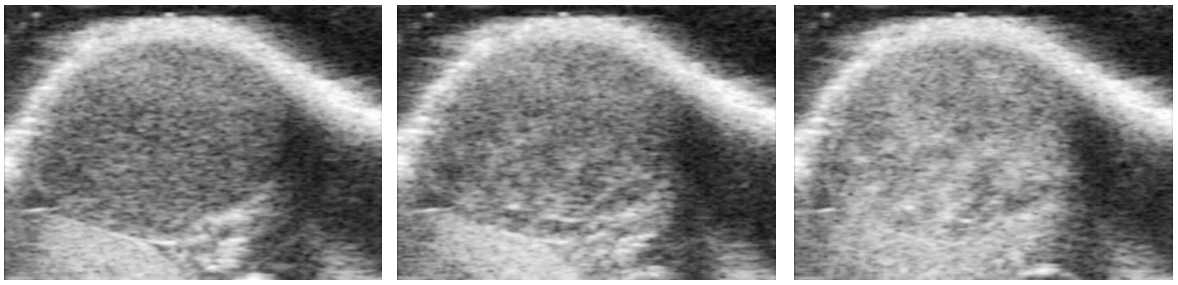

**Figure 1:** The first image is acquired before UCA injection, the second is after UCA injection during contrast-filling stage and the third is after contrast-filling stage.

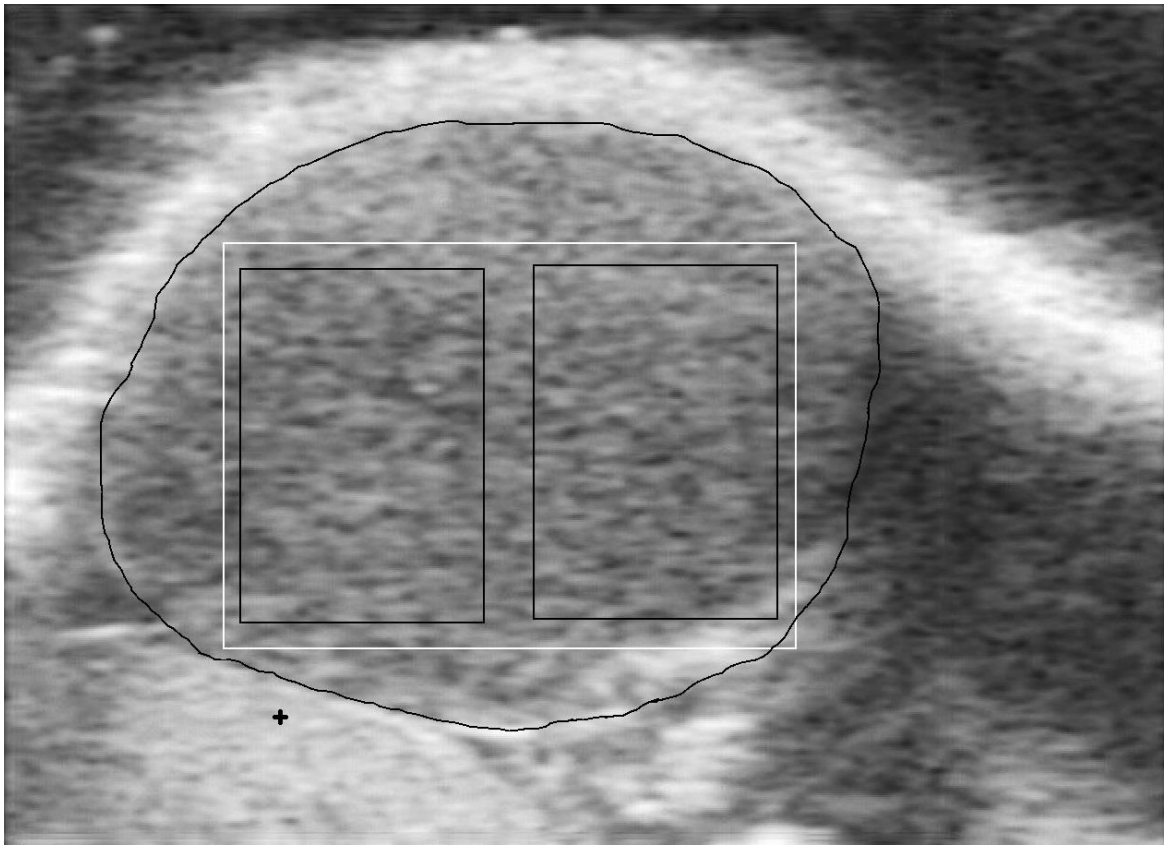

**Figure 2:** The first image of the tested 2D image sequence with delineated important areas.

## 3. METHOD

The basis of the method is an intensity-based algorithm that compares two regions of an image ($n$) with that of an image ($n$+1). By observing the images there was subjectively found out the rotation movement of the tumor with the center of rotation outside the tumor area. The algorithm was developed in accordance with the predetermined information.

As aforementioned, the algorithm executes the registration of images for two regions. The registration is executed for each region separately. Thus, the output of the algorithm is two registered image sequences that are then combined into one image sequence. In figure 2, there are the regions (left and right) delineated as black rectangles. Their size is the same (193×133 pixels). The registration part of the algorithm is the same for both regions and is described in the following steps. At the beginning, the center of the rotation (CoR) is subjectively selected (marked in figure 2 as a cross). Subsequently, the square grid of potential points of the CoR is created with the point distance of 10 pixels around the selected CoR (the point distance of 10 pixels was found small enough). The whole image is progressively rotated about each potential point of the CoR for angles

from -2° to +2° with the step of 0.01°. The algorithm compares pixels of the rotated image falling into the region with that of already-registered image on the basis of correlation coefficient criterion ($C_{CC}$).

$$C_{CC}(A,B) = \frac{\sum_m \sum_n (A_{mn} - A_r)(B_{mn} - B_r)}{\sqrt{\left(\sum_m \sum_n (A_{mn} - A_r)^2\right)\left(\sum_m \sum_n (B_{mn} - B_r)^2\right)}}, \quad (1)$$

where $A$ is the region of the reference image, $B$ is the region in the unregistered image, $A_r$ and $B_r$ are the corresponding mean values [3]. Each image is registered to previous already-registered image. This type of the registration was chosen due to the high speckle noise level.

The parameters of the registration are the position of CoR and the angle of the rotation (AoR). The computed registration parameters are different for the left and right region. Therefore, images registered using the left region (LR) differ from images registered using the right region (RR). LF registered images and RR registered images cannot be simply combined together. The area between the regions serves as a combining part. That part is registered according to the parameters of both regions.

## 4. RESULTS

The effect of the registration is to see in figure 3 and 4. In figure 3, the similarity of neighboring images in the sequence is expressed using the correlation coefficient. However, in this case, the effect of the registration is not visible enough and hence, in figure 4, the similarity is expressed as average pixel intensity difference (APID). In both latter figures, the contrast-filling stage is highlighted. Especially in figure 4, we can see the positive effect of the registration. The proposed algorithm adapts well to the large changes of pixel intensities during the contrast-filling stage because no extreme fluctuations occur in the waveform of the curve of the registered image sequence. According to the APID, the similarity of neighboring images was improved by ≈ 0.32 at average after the registration. The improvement of the similarity seems apparently negligible but this is caused by the high speckle noise level.

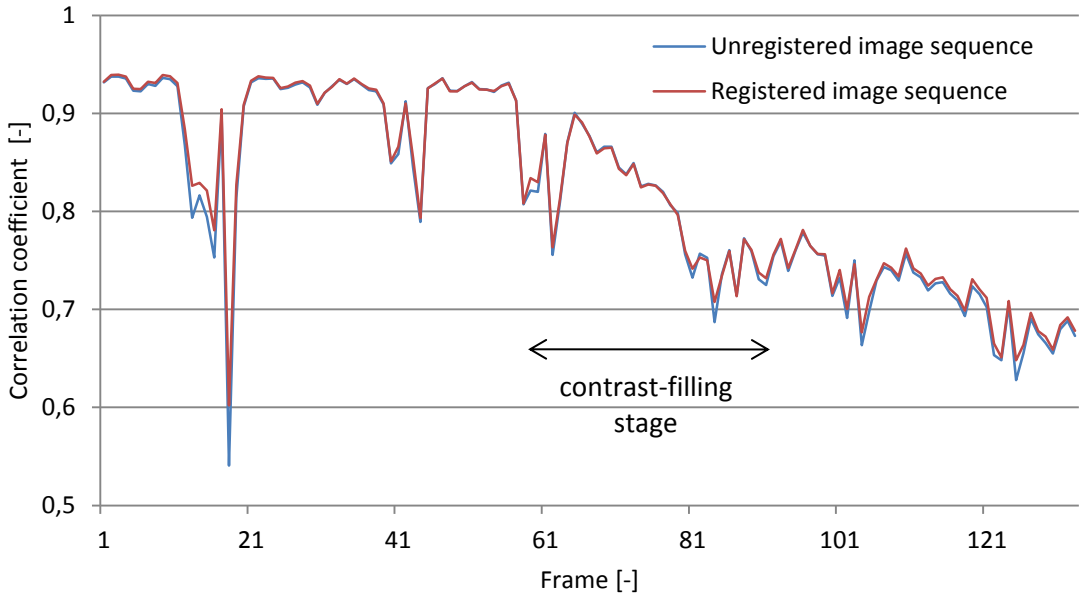


**Figure 3:** Correlation coefficient between white rectangle areas in consecutive frames.

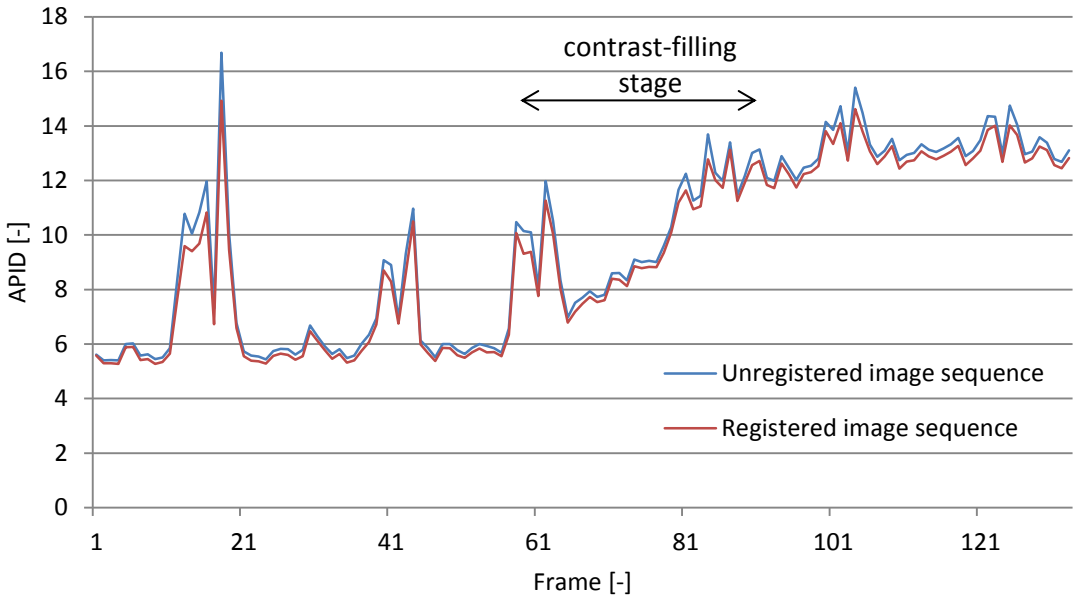


**Figure 4:** Average pixel intensity difference (APID) between white rectangle areas in consecutive frames.

In figure 4, curves contain six peaks that indicate tissue movements induced by breathing. The registration process consists predominantly in the rotation of an image. Figure 5 shows the functionality of the registration algorithm. The six peaks of the unregistered image sequence curve anti-correlate with the negative peaks of the left and right region AoR curves. The left and right region AoR curves represent the angles of the rotation of an image for the left region and right region, respectively. The waveforms of the curves are not influenced by the contrast-filling stage. This fact confirms the robustness of the algorithm to the large changes of pixel intensities.

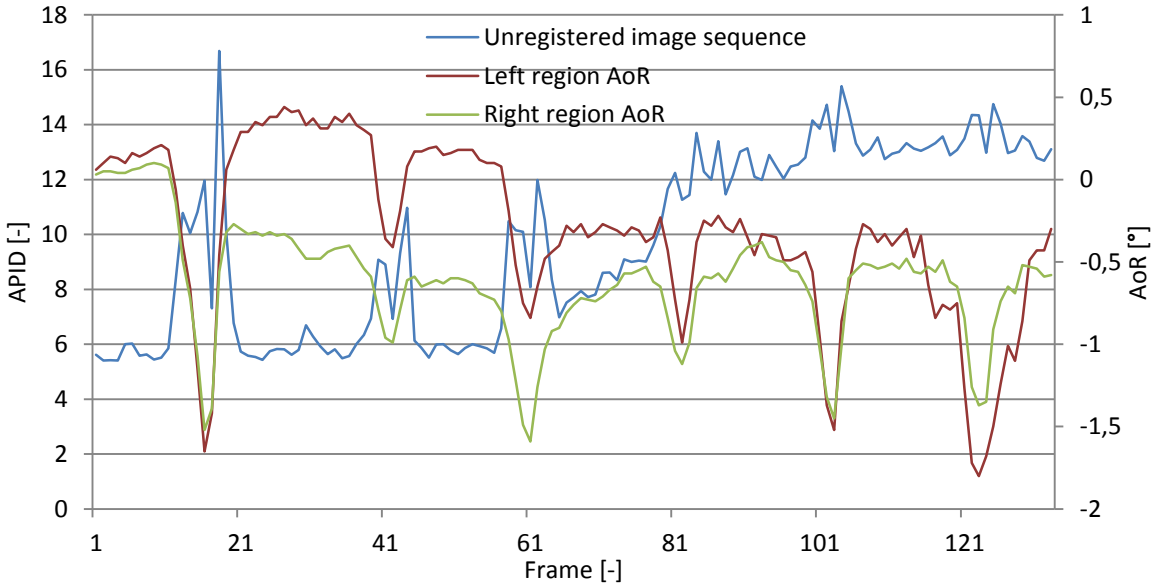


**Figure 5:** The comparison of the AoR of the left and right region with the PID of the unregistered image sequence.

The registration of the sequence is executed successively (image by image). This registration type suffers from a cumulative error. The cumulative error of my registration algorithm is insignificant because the registered image sequence curve copies the waveform of the unregistered image sequence curve in whole length (Fig. 4) and the difference between these curves is greater during the

breathing phase (tissue movement). Due to these findings, the registration process is not very corrupted by the speckle noise as well.

## 5. CONCLUSION

The proposed method was developed and tested in MATLAB®. Reached results proved the functionality of the method. The algorithm detected and suppressed tissue movements in spite of high speckle noise level. The algorithm is also very robust to contrast-filling stage.


## ACKNOWLEDGEMENT

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