ESTIMATION OF GROWTH OF OVARIAN FOLLICLES USING RIGID AND ELASTIC ULTRASOUND IMAGE REGISTRATION

Sebastijan Šprager, Boris Cigale and Damjan Zazula
System Software Laboratory, Faculty of Electrical Engineering and Computer Science
Smetanova ulica 17, 2000 Maribor, Slovenia

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Abstract: In this paper, a method for assessment of the ovarian follicle growth is presented. 3D ultrasound volumes of ovaries are processed. Ovarian follicles are shown as hypoechogenic areas in the cross-section images. In first phase, global translations and rotations of two observed follicle constellations from two consecutive ovary examinations are detected. In second phase, detailed local deformations are estimated using elastic registration. The proposed method has been tested using artificial simulated models of ultrasound images of ovaries. Preliminary results shows the proposed method is efficient and reliably detects deformations ovarian follicles cause by their growth.

1 INTRODUCTION

Ultrasound plays a very important role in medical diagnostics. Non-invasive observations of vital parts of human body and their changes are feasible. Our research was focused on observation of deformations of ovarian follicles due to their growth using ultrasound examinations. The growth and decaying of ovarian follicles can be observed using 3D ultrasound images today, acquired also in several consecutive examinations of the same woman. Speckle noise deteriorates ultrasound images and complicates visual observation of such growth changes. Our goal was to build a method to compare two 3D ultrasound volumes and estimate possible differences between the follicles and indicate those deformations that result from the growth or decaying of an ovarian follicle.

Most of published researches deal with a large number of 3D ultrasound images acquired in short and successive time intervals. An example of such a method is presented in (Chandrashekara et al., 2004), where the MR images are marked with points for alignment in a registration. After the registration, changes in the position of those points indicate deformations of observed tissues.

Changes in image contents can be sought for by image registration. Image registration belongs to the fundamental methods of medical image processing. By definition, image registration is a process of overlaying two or more images that show similar scene, but they are acquired at different times, different perspectives, or with different sensors (Zitova and Flusser, 2003). Matching of registered images should be optimal in the sense of finding the best fit between two images when using geometric transformations.

Image registration methods are divided in two larger groups: rigid registration methods and non-rigid or elastic registration methods (Maintz and Viergever, 1998). Rigid registration methods allow only affine geometric transformations, mostly only limited to rotations and translations. Transformations are defined global for the whole image. Elastic registration is searching for the best fit between two images by compensating local deformations, so that the difference between the two images when aligned is minimal according to a chosen metric (Crum et al., 2004).

Our situation is more complicated than the published solutions. If a set of images with small deformations is available, we can determine these deformations by observing only the differences between chronologically successive images. But such iterative method fails, when only few images are available, such as ovarian examinations

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separated by a longer time interval and, thus, differing by large changes.

This is the starting point of our research. To better understand the boundaries, we modelled the described large changes in simulated ovarian follicle ultrasound volumes. The approach is described in Section 2. In Section 3, we present the methodology proposed for the detection of the ovarian follicle growth. The obtained results are analyzed in Section 4. The paper is concluded in Section 5.

2 SIMULATION MODEL FORMULATION

In Section 1, we presented the most common concept in searching for the tissue deformation by using a registration of successive images. When the ultrasound recordings do not contain highly similar consecutive images, different solutions are necessary. In the case studied in this paper, two 3D ultrasound images of ovaries are acquired at different times. They are considered an initial and a final volume. The differences between those images can be considerable; it is possible, that some of the follicles grow fast, some of them are slower, some of them decay, and even new follicles can appear sporadically.

The main task when searching the growth changes is to verify the similarity between two constellations of follicles by comparing, i.e. registering them respectively. We presume that a combination of a rigid and an elastic registration can point out the deformations of follicle shapes due to their growth. The rigid registration is supposed to insert the volume of the initial follicle into the final volume spatially centralised. The remaining differences between the two volumes must, then, correspond to the volume differences of the compared follicles. We suggest to locate the differences by using elastic registration.

The aforementioned suppositions do not hold in general. Therefore, we have to define and took into account some realistic constraints. The most important says that follicles grow in all spatial directions with the same probability. In such cases, a rigid registration of two constellations of follicles, which aligns the follicle centroids and axes, inserts the initial follicle volume into the changed, increased volume in such a way that the differences of the volumes indicate the follicle growth. Our experiments followed, and verified, this idea.

The simulations carried out are described in the next subsection. A description of a two-step detection of follicle growths follows next.

2.1 Simulation of Ultrasound Volumes

For statistical evaluation of proposed method we would have to accomplish statistical relevant amount of trials, for example Monte Carlo methodology with included set of all possible changes between two 3D ultrasound images of ovarian follicles. This would lead in an increased time complexity of simulation – creation one of the simulated 3D images lasts few hours, as long as elastic registration.

To achieve the most efficient validation of method for growth assessment, the models of ultrasound volumes of ovarian were built with use of simulation. One model represents a set of five simulated ultrasound volumes with different constraints. Those volumes represent volumes acquired in successive time intervals. The presented models were built with purpose to determine what are the maximum deviations of the follicles from the follicles in the initial volume for efficient estimation of their deformation.

In each model an initial volume represents the source for other four volumes. The second volume is deformed version of first one, the third volume is deformed version of second one, etc. This kind of deformations represents growth of ovarian follicles that appear in the real world. Different deformation types are used for each model. The properties of model deformation are described in the next subsections.

2.1.1 Model Construction

Ovarian follicles are in initial volume represented as ellipsoids in 3D space, corresponding to basic shape of ovarian follicles. Generated ellipsoids were then deformed with local transformation; each reference point of the mesh, which describe an ellipsoid, was translated for a small vector, where each component was generated from normal random distribution within interval ±10% according to the size of the ellipsoid. The deformed ellipsoids are very similar to the real ovarian follicles. After generating volumes of ellipsoids, the ultrasound noise was applied to each volume with use of program simulator called Field II (Jensen, 1996). The size of each volume was $100 \times 100 \times 100$ voxels.

In the same manner we created other four volumes that stand for final volumes of follicle growths. Every final volume is a version of the initial volume, deformed with global and local deformations. These deformations are a global rotation, additional rotations of individual follicles, local deformations as a consequence of growth or decaying of follicles, and additional local deformations with random translation of the reference points of the ellipsoids, as described in previous paragraph. Constraints are described in the next subsection.

2.1.2 Constraints

For each volume in the model we applied global rotation according to its previous state. Each angle of rotation was selected randomly from normal distribution within interval ±10°. Global translation was not applied. Each of ovarian follicles were rotated individually with angles selected randomly from normal distribution within interval ±10°. Also in this case translation was not applied.

Local deformations caused by the growth or decaying of ovarian follicles are represented by the variations of the size and shape of each follicle. The size of each follicle varies uniformly in all directions, which illustrates the real growth of ovarian follicles. The amount of variation is selected randomly within the interval from 1% to 20% of the follicle size for increases, and within the interval from -1% to -20% of the follicle size for decreases.

2.1.3 Model Description

For our experiment, two models of ovarian follicles were created. Model 1 contains three round-shaped ovarian follicles. Follicles *f1* and *f2* have similar size, follicle *f3* has a size of one third of the size of *f1* or *f2*. The changes applied to the follicles cause *f1* increase, *f2* and *f3* decrease, while *f3* eventually almost disappears. Model 2 also contains 3 follicles that are in this case oblong-shaped. Follicles *f1* and *f2* have similar size, whereas the follicle *f3* has size of 80% of *f1* or *f2*. Follicle *f1* grows, follicles *f2* and *f3* decay. Also in this model *f3* almost disappears eventually.

3 METHODOLOGY

As mentioned, the proposed method for detecting discrepancies between two ultrasound volumes is based on a two-step registration. In the first step, we apply the rigid registration between the initial and final volume. The aim of this registration step is to compensate global differences (rotation and translation of the whole volumes of ovarian follicles). Different probe directions, i.e. angles of acquisition can cause such differences. Furthermore, we have to recognise local differences that correspond to the growth or decaying of ovarian follicles. In an ideal case, the rigid registration locates the basic position of the initial volume within the final volume, because the final volume grow from the initial volume in all spatial directions with the same probability.

Our experiments deploy simulations local follicle deformations. For detecting these, we applied elastic registration of initial and final volumes right after rigid registration. It has to be emphasised that local follicle deformations may significantly influence the error of rigid registration (from a global point of view). The error appears as an additional contribution to the actual local differences. Again, our purpose was to discover the amount of local deformations, i.e. the follicle growth.

The proposed two-step detection method can be described by the following equation:

$$\{V^1, V^i\} \xrightarrow[registration]{rigid} V^{1i} \xrightarrow[registration]{elastic} V_e^{1i}, \quad (1)$$

where V^1 represents the initial volume, V^i represents the *i*-th final volume ($i = \{2,3,4,5\}$), V^{1i} represents the initial volume registered using the rigid registration on the *i*-th volume, and V_e^{1i} stands for the same volume after the elastic registration applied. Each performance of the proposed method is named a trial. The same labeling and naming convention will be used in the section with results.

3.1 Rigid Volume Registration

We used a new method for rigid registration which registers two different constellations of ovarian follicles (Cigale, 2007). Rotation and translation are handled separate in 3D frequency space. We search the rotation first and only then the translation.

Rotation is being sought in the amplitude part of frequency spectrum by applying spherical correlation. The rotation angle is found where the two frequency amplitude spheres have best fit. Reliability of the method increases through consecutive iterations at different distances of the observed frequency spheres from the coordinate system origin. The translation between the compared volumes is calculated by generalized cross-correlation. The obtained transformation matrix is improved by the progressive approach algorithm (Cigale, 2007).

Cross-correlation based on spheres in 3D frequency space becomes unreliable when large differences appear between the compared volumes (for example, when new follicles appear). The problem is solved by comparing the two chosen frequency spheres of initial and final volume in a multiresolution scheme. The volumes are processed by wavelet transform, using the Mexican hat mother wavelet. Volume registered is based on wavelet coefficients, descending from higher to lower scales. The method details are revealed in (Cigale, 2007) and (Cigale and Zazula, 2004).

Rotation in 3D is described with 3 angles. We implemented a special transformation to transform the 3 angles into one single spatial angle denoted by Θ. This angle between two rotations is defined by quaternions:

$$\Theta = 2\arccos(|q_1 q_2|), \tag{2}$$

where $|q_1 q_2|$ represents dot product of quaternions for two observed rotations. Quaternion q we describes a rotation around unit vector $\boldsymbol{v}$ for angle α as $q = (\cos(\alpha/2), \boldsymbol{v}\sin(\alpha/2))$ (Cigale, 2007). Vector $\boldsymbol{v}$ is taken as space diagonal, so that all the applied rotations are limited to this diagonal.

3.2 Elastic Volume Registration

Rigidly registered initial and final volumes enter an elastic registration in the next algorithm step. We used an approach based on locally invariant speckle-noise mean in compared ultrasound volumes (Yue et al., 2009), (Šprager and Zazula, 2008). The difference between compared volumes can be described with the following deformation model:

$$\mathbf{u}(\mathbf{x}) = \mathbf{x} + \sum_{\mathbf{k}\in\mathbb{Z}^3} \mathbf{c_k}\,\beta^3\left(\frac{\mathbf{x}}{\mathbf{h}} - \mathbf{k}\right), \tag{3}$$

where $\mathbf{x}$ designates a voxel, $\mathbf{c_k}$ deformation parameters, and h the distance, in voxels, between two B-spline knots, denoted by β^3 (Kybic and Unser, 2003).

Optimal elastic registration is being sought by modifying the deformation parameters that affect the surroundings of voxel $\mathbf{x}$. The appropriate deformation parameter values are being sought by the L-BFGS-B optimization algorithm (Zhu et al., 1997). Objective function is represented in the following equation:

$$\mathrm{E} = \frac{1}{\mathrm{N}} \sum_{\mathbf{x}\in\mathbb{Z}^3} \Big(\ln\big(\exp\big(2\mathbf{r}(\mathbf{x})\big) + 1\big) - \mathbf{r}(\mathbf{x})\Big), \tag{4}$$

where $\mathbf{r}(\mathbf{x})$ represents a difference between initial and final volume (Yue et al., 2009). The registration procedure is iterative; the initial volume is fitted the to final volume. The procedure terminates when differences between the volumes decrease below a predefined threshold.

Elastic registration computes a deformation field $\boldsymbol{u}(\mathbf{x})$, which contains displacement vectors for each voxel. We used those displacement vectors as the estimate of deformations, that probably result from the ovarian follicle growth.

3.3 Efficiency Estimation

For estimation of efficiency of ultrasound image registration, a $\rho^{(1)}\rho^{(2)}$ metric is suggested in (Cigale, 2007), (Cigale and Zazula, 2004). The ratio $\rho^{(1)}$ compares the intersection volume of the two registered volumes to the final volume. The ratio $\rho^{(2)}$ compares the intersection volume of the two registered volumes and the initial volume. The ratio values lie between 0 and 1. Value 1 represents fully covered volumes. $\rho^{(1)}$ also corresponds to sensitivity and $\rho^{(2)}$ to specificity. The larger their product, the better is the resulting registration matching.

We used this efficiency measure to evaluate the performed registrations, both the rigid and elastic ones.

4 RESULTS AND DISCUSSION

As explained in section 2, for evaluation of our method we have built 2 models. Each model contains 5 volumes acquired in successive time intervals – first volume is called as initial, other 4 volumes represent final volumes. The deformation of the follicles is growing with increasing of time interval. For each model 4 trials were performed. The trial was performed between initial volume and each of the final volumes. The main purpose was to find out the maximum deviation of the size and shape of the follicles for accurate estimation of the deformations.

As explained in Section 2, an efficient rigid registration is the main precondition for an accurate detection of volume changes. It has to result reliably aligned centroids of initial and final volumes, and their axes as well. Therefore, two metrics are presented as a result which shows the efficiency of rigid registration.

In Table 1, the difference between the detected rotations of the compared volumes are presented. Rotation angles estimated from rigid registration must coincide with the actual rotation angles generated for the simulated ultrasound volumes. The difference between those two rotation is expressed with angle Θ, as described in Subsection 3.1. The smaller the angle, the better the result of rigid registration. The angles in the trial 2, 3, 4 and 5 deploying model 1 are acceptable, only the 5-th experiment with model 2 differs significantly.

Table 1: Angle Θ between two rotations retrieved from transformation matrix T_s of simulated volumes and transformation matrix of rigid registration T_r for each trial. The smaller the angle, the better the result of rigid registration.

	Model 1	Model 2
$\Theta(T_s^{12}, T_r^{12})$	10.76209	6.35026
$\Theta(T_s^{13}, T_r^{13})$	22.54942	38.26064
$\Theta(T_s^{14}, T_r^{14})$	22.05884	16.46824
$\Theta(T_s^{15}, T_r^{15})$	177.90060	31.03795

Table 2: Distances, in voxels, between the follicle centroids, C, of the final volume and rotated initial volume after rigid registration for each trial.

		Model 1	Model 2
$d(C^2, C^{12})$	*follicle 1*	11	4
	follicle 2	5	4
	follicle 3	6	3
$d(C^3, C^{13})$	*follicle 1*	5	3
	follicle 2	3	5
	follicle 3	3	2
$d(C^4, C^{14})$	*follicle 1*	66	3
	follicle 2	1	3
	follicle 3	2	7
$d(C^5, C^{15})$	*follicle 1*	73	7
	follicle 2	2	11
	follicle 3	3	4

The second and the most important metric is difference between centroids of final volume and rotated initial volume after rigid registration. From Table 2, we can see that the distance between centroids grows with the increased time distance between the recordings of the compared volumes. In both models, the only problematic follicle is *f1* in the 4-th and 5-th trial with the first model, the follicle that is disappearing. These results cannot be taken as properly recognised positions. If an error threshold is set at 5%, at least the results of the first 3 trials can be considered correct.

The elastic registration which followed the rigid one revealed local differences between initial and final volume. In Figure 1, all steps of the proposed method is shown on the example. The slices of model 2 are presented. Slices are positioned in the centroids of all three follicles. Differences as they develop through the phases are clearly visible.

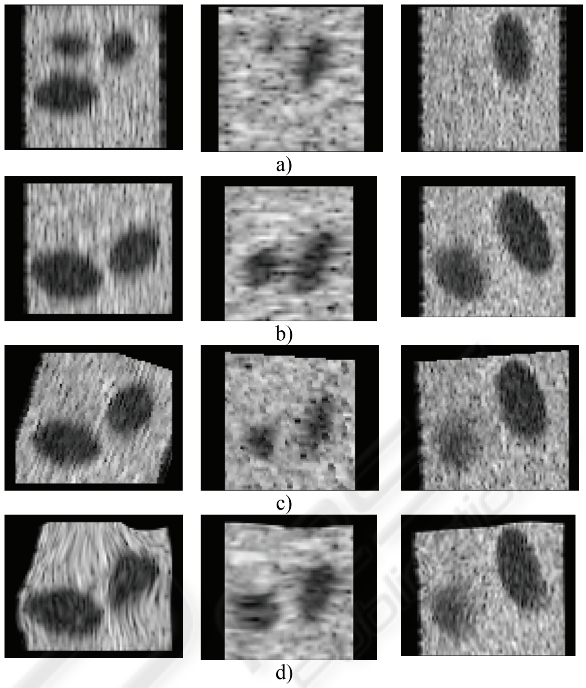

Figure 1: Slices of ultrasound volume as examples through the steps of deformation estimation method. Row (a) shows initial volume, b) shows final volume, c) shows final volume after rigid registration and d) shows final volume after elastic registration. Triples of slices correspond to the intersections through the ultrasound volumes at the positions of the centroid of three generated follicles.

Table 3: $\rho^{(1)}\rho^{(2)}$ metric for both models.

		M1r	M1e	M2r	M2e
$\rho^{(1)}\rho^{(2)}$ $V^1 \rightarrow V^2$	*f1*	0.0692	0.0861	0.6426	0.7826
	f2	0.5019	0.5478	0.6552	0.7673
	f3	0.3801	0.5129	0.5421	0.6376
$\rho^{(1)}\rho^{(2)}$ $V^1 \rightarrow V^3$	*f1*	0.0385	0.0504	0.5855	0.5890
	f2	0.4956	0.5636	0.5230	0.5307
	f3	0.2869	0.4554	0.5765	0.5829
$\rho^{(1)}\rho^{(2)}$ $V^1 \rightarrow V^4$	*f1*	0.0000	0.0000	0.4641	0.4658
	f2	0.4697	0.6282	0.4676	0.4700
	f3	0.7037	0.6996	0.3626	0.4020
$\rho^{(1)}\rho^{(2)}$ $V^1 \rightarrow V^5$	*f1*	0.0000	0.0000	0.3701	0.7313
	f2	0.5596	0.5274	0.3194	0.4320
	f3	0.5830	0.7258	0.3372	0.4013

The efficiency of elastic registration is also estimated by two metrics. Metric $\rho^{(1)}\rho^{(2)}$ is described in Subsection 3.3. Results are shown in Table 3. It is clear that the value of $\rho^{(1)}\rho^{(2)}$ ratios worsen when the time distance between the volumes increases, what under the assumption, that the centroids and axes of the follicles are aligned, represents the difference between two observed follicles.

Table 4: Differences, in voxels, in the follicle axes lengths, comparing the calculated follicle positions after both registrations with their initial volumes. The smaller the difference, the smaller the error of the estimation of the follicle local difference.

		Model 1			Model 2		
$d(a_s^{12}, a_e^{12})$	*f1(x,y,z)*	14	1	4	1	2	3
	f2(x,y,z)	12	2	5	0	0	1
	f3(x,y,z)	3	1	2	0	0	0
$d(a_s^{13}, a_e^{13})$	*f1(x,y,z)*	17	3	6	1	0	2
	f2(x,y,z)	14	1	5	1	1	0
	f3(x,y,z)	4	1	2	2	2	0
$d(a_s^{14}, a_e^{14})$	*f1(x,y,z)*	20	6	9	2	2	5
	f2(x,y,z)	16	3	9	1	2	1
	f3(x,y,z)	5	2	4	1	0	2
$d(a_s^{15}, a_e^{15})$	*f1(x,y,z)*	24	6	11	8	8	9
	f2(x,y,z)	23	7	14	0	0	2
	f3(x,y,z)	6	3	6	0	2	1

Table 4 shows a metric which represents the error of the local difference estimation. The error is expressed as the difference in voxels between lengths of overlapping axes of the follicles after the simulation and after the performance of the proposed methods. Follicles were are aligned in the centroids and in all 3 coordinate directions. As expected, errors grow when the time interval between the compared volumes increase. As we already seen in the Table 2, follicle *f1* in model 1 is problematic due to its shape, but the estimation for other two follicle is quite accurate (errors between 5% and 12%). The results for model 2 are entirely better. In the second trial, the error is practically negligible, and also by the last one reaches an error as low as only about 3%. This situation shows that the estimation accuracy strongly depends on the shape and deformation intensity of the ovarian follicles. If an error threshold is set at 5% and centroids and axes are correctly aligned, the results of the first 3 trials can be considered correct, what means that in our case the difference between follicles does not exceed 20% of their size.

5 CONCLUSIONS

The proposed method for ovarian follicles deformation detection is implemented by using a rigid and an elastic registration of 3D ultrasound images. Firstly, we detect rigid deformations of ovarian follicles represented with rotation angles. Finally, a detection of local differences between follicles is presented.

We have discovered that the performance of the proposed method depends on the shape and the deformation intensity of the compared volumes. As could have been expected, the results are better when the follicle changes are smaller. Our experiments confirm the proposed method can detect the growth changes of follicles if the differences between follicles in the two observed constellations do not exceed for about 20% of their size.

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