

An improved wavelet-based contralateral subtraction algorithm

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Abstract—Contralateral subtraction is an image processing technique aimed to enhance asymmetries in chest radiographs. Since malignant processes often result in asymmetrical lesions, a computer aided diagnostic system capable of enhancing asymmetries on these images could support the diagnostic procedure. The technique itself consists of registration of the two lung areas, and subtraction of the registered images. Contralateral subtraction is therefore essentially a registration problem, a field that has been widely researched offering various solutions to the problem at hand. One of these solutions is wavelet transformation, a multiresolution method that has a potential not fully unlocked by previous methods. We propose a contralateral subtraction scheme based on an elastic registration algorithm in the wavelet domain, using dual tree complex wavelet transform. By registering only the low frequency components of the images, the resulting transformation will be inherently regular, without relying on conventional regularization methods. We demonstrate the effectiveness of this concept by applying it to a contralateral subtraction problem, verifying the algorithm with synthetic tests as well as chest radiographs from the JSRT public database. These results show an increased sensitivity of nodule detection, indicating that the proposed method is a valid alternative to other known registration methods.

I. INTRODUCTION

One of the most common types of cancer is lung cancer, in terms of both mortality and incidence. It is well-known, that the effectiveness of the treatment is mostly affected by how advanced the disease is. Regular screenings would assure early detection, while producing large amount of chest radiographs to be analyzed. Procession of these images could be made easier through computer aided diagnostic (CAD) systems, that would assist the diagnostician using automated image processing techniques, such as de-noising, finding asymmetries or even pulmonary nodules[1]. One of these techniques is called contralateral subtraction (c-sub) – a method capable of analyzing the symmetry of the lungs. Malignant lesions in the lungs are characteristically asymmetric, thus symmetry-analysis provides a possibility to emphasize crucial information regarding the diagnosis.

The analysis consists of registering of the left and right lungs, and subtracting the two registered images, so that on the resulting image only asymmetrical features remain. Studies indicate that such implementations might improve the detection chances of malignant lesions [2] [3]. Methods

of solving the image registration problem, i.e. aligning the left and right lung fields so that they overlap, have been widely researched, and used in a number of medical imaging applications – such as CT, PET, or MRI – and also in various fields of computer vision and remote sensing.

Some of these methods utilize a multiresolution approach, handling different frequencies of the analyzed images separately. A possible tool in this case is wavelet transform, an integral transformation capable of separating the different frequency components of the image. The method has been used in many aspects of image processing, including general image registration [4] and medical applications [5], even in the case of chest radiographs [6]. These methods, however, do not fully utilize the possibilities provided by wavelet transform, since – as it will be demonstrated later – multiresolution analysis also provides a means to regularize the transformation.

In this paper we propose an improved method to exploit a further advantage of wavelet transform in addition to multiresolution analysis. After a brief introduction to the problem we will propose registering only low-frequency wavelet components to ensure the regularity of the transformation. The paper will demonstrate the effectiveness of the proposed method by applying it to contralateral subtraction. The verification of the method was performed via integrating the implemented c-sub scheme with an existing CAD-application, and evaluating overall improvement.

II. BACKGROUND AND MOTIVATION

Registration in general can be solved with two possible approaches, image based or feature based [7]. Although both methods are relevant in medical applications [8], in the following we focus on the former approach. Image – or texture – based methods aim to find a transformation between the two images, representing them as vector-scalar functions. The transformation $\mathcal{T}$ sought between the reference image or template $t(\mathbf{x})$ and the registered image or study $s(\mathbf{x})$ can be formalized as a vector-vector function $\Phi(\mathbf{x})$, $\mathbf{x}$ being the pixel coordinates. The problem formulation in case of elastic transformations:

$$t(\mathbf{x}) = \mathcal{T}\{s(\mathbf{x})\} = s(\Phi(\mathbf{x})) = s(\mathbf{x} + \mathbf{u}(\mathbf{x})), \quad (1)$$

where $\mathbf{u}$ is the so called displacement field, which maps the pixels of the two images on another. Finding this displacement field is typically done using an optimization approach: defining a similarity measure as a cost function, and searching for the displacement field yielding a minimal cost function value with an optimization algorithm, e.g. steepest descent, conjugate gradient etc.

These methods provide a displacement field that renders the two images identical, which is in most cases not desirable. The resulting transformation has to align the two images to each other without extremely distorting them. Extreme distortion in this case means, that the distortion not only corrects the unknown transformation, but introduces further artifacts as well, new lesions for instance, or expand existing ones, in other words it has to be regular. Regularity of the displacement field can be ensured using viscous or elastic deformable models, that limit the applied distortion similarly to viscous or elastic materials [9].

Wavelet-based and other multiresolution methods use several image representations that correspond to different frequency intervals. While this approach is effective in improving convergence and quality of fitting by registering the images gradually from coarse to fine scales, it still requires regularization. Regularity, on the other hand, is only connected to low frequencies. A transformation that makes the two images more similar – according to a similarity measure – and also has only low-frequency components is bound to be regular. This raises the question if registering only the low-frequency – or approximation – coefficients of the wavelet transformed displacement field would result in an inherently regular transformation, without any further regularization.

III. MATERIALS AND METHODS

A. Application structure

The proposed c-sub scheme divides the task to four main steps, as illustrated on figure 1.

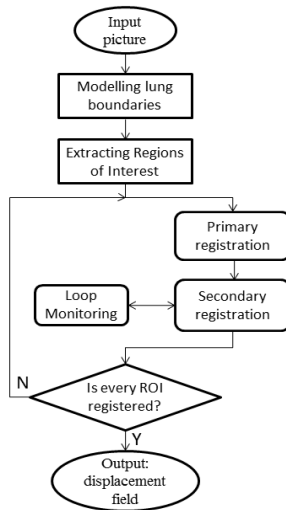


Figure 1. Layout of the c-sub algorithm

Firstly, the boundaries of the lungs have to be determined to identify the areas to subtract. The proposed algorithm will be a part of a complex CAD system, which is capable of determining the pixel coordinates of lung boundary points. The received boundary points are then simplified in form of a polygonal lung model, so that lung boundaries are represented by straight lines.

To provide a possibility to separately analyze lung segments, the area inside the determined boundaries is further segmented into regions of interest (ROIs), which will then be individually registered. This approach also overcomes the problem caused by the cardiac silhouette – the heart muscles overshadow some of the left lung area, resulting in a large asymmetrical feature. Furthermore, as we later show, this approach is computationally less expensive than registering the whole lung at once – especially considering parallelizability. ROI registration incorporates two steps: finding the contralateral ROIs and registering them using a dual tree complex wavelet transform based optimization algorithm.

B. Registration algorithm

Finding the contralateral equivalents of the designated ROIs is essentially compensating a large displacement and a small rotation, i. e. a rigid transformation between the two regions. In case of negligible rotations the easiest way to compensate this kind of transformation is based on the $\gamma(u, v)$ normalized cross-correlation coefficients as follows:

$$\gamma(u, v) = \frac{\sum_{x,y} [s(x, y) - \bar{s}_{u,v}][t(x-u, y-v) - \bar{t}_{u,v}]}{\sigma_s \sigma_t}, \quad (2)$$

where

$$\sigma_s = \sqrt{\sum_{x,y} [s(x, y) - \bar{s}_{u,v}]^2},$$

$$\sigma_t = \sqrt{\sum_{x,y} [t(x-u, y-v) - \bar{t}_{u,v}]^2},$$

and $\bar{s}_{u,v}$ is the mean value of a template sized area of the study shifted to (u, v) , and $\bar{t}_{u,v}$ is that of the template.

After flipping the ROI in question, our algorithm reflects the ROI to the other side of the chest, so that the reflected – contralateral – ROI will have the same relative position to the polygonal borders, as the original. After that a search is performed in a region around the reflected image, calculating the $\gamma(u, v)$ coefficients in that region. The region with maximal correlation will be defined as the contralateral ROI, as seen on figure 2.

The secondary registration transforms the selected ROI using the contralateral ROI as template. The following cost function is minimized by a steepest descent algorithm in the wavelet domain (with the above notation):

$$J(\mathbf{u}) = \frac{1}{2} \int \{s(\mathbf{x} + \mathbf{u}(\mathbf{x})) - t(\mathbf{x})\}^2 d\mathbf{x}. \quad (3)$$



Figure 2. Result of the contralateral ROI detection. The original ROIs are green, the cross-correlation based search is done in the region inside the red box, the resulting contralateral ROI is yellow.

The algorithm calculates the gradient $\nabla J(\mathbf{u})$ in every step and uses the approximation coefficients of its wavelet transform to change the approximation coefficients of the displacement field. If $\mathbf{U}_a^n$ notes the approximation coefficients of the wavelet transform of $\mathbf{u}$ in the n -th step:

$$\mathbf{U}_a^{n+1} = \mathbf{U}_a^n + \eta \frac{\partial J^n}{\partial \mathbf{U}_a^n}. \quad (4)$$

The displacement field is inverse transformed after that, and applied again in accordance to eq. 3 to calculate J^{n+1} . Since gradient descent algorithms can take long to converge, an adaptive step size η is used for minimizing run times.

C. Dual Tree Complex Wavelet Transform

Most wavelet based registration algorithms use discrete wavelet transform (DWT) to decompose the images. However, dual tree complex wavelet transform (DTCWT), an improved variant of DWT using complex wavelets, was shown to be a powerful tool for multiresolution image analysis, having numerous advantages over its real variant [10].

DTCWT differs from DWT insofar as its mother wavelet is complex, so that the imaginary part is the Hilbert transform of the real part. This does not require different calculation methods, the same calculations need to be done twice, once for the real, and once for the imaginary part. In two dimensions this means four times as much calculation as in the case of DWT. Computational expense is rewarded with the compensation of some problems that DWT has.

Aside aliasing and shift variance, the poor directional selectivity of DWT can also be overcome by using complex wavelets, improving registration performance [11] [12]. Having regard to the above, a DTCWT based registration algorithm has also been implemented besides the standard DWT.

D. Early termination

Termination usually occurs if convergence is reached, but given that the two images are essentially – contrary to most cases – not the same, registration can lead to a distorted image.

Firstly, unsatisfactory primary registration results in a distortion. If the remaining rigid component is too large, and if the inwards expansion of the ROI borders can reduce the cost function, the resulting displacement field covers the area with a blur. This phenomenon can be seen on figure 3. Major intensity differences between images can also lead to distortion. These can be interpreted as a loss of information, meaning that in some cases secondary registration is ill advised. These scenarios can easily be detected by monitoring displacement vector norms. If distortion is detected, step size is decreased, and if that was not the problem, registration of the distorted ROI is stopped.

IV. RESULTS

The functionality of the c-sub scheme depends mostly on whether the registration is correctly performed. It is therefore advised to test the registration algorithm separately using synthetic, manually created tests before verifying the complete c-sub algorithm.

A. Synthetic tests

The first synthetic test was performed applying a manually created displacement field – a 10 pixel translation upwards. As the result indicates on Figure 4, the method is basically functional.

After that, to determine how segmentation of the lung area affects run times, as well as to test basic functionality, a large scale synthetic test was used. We applied 200 different displacement fields on the same image, and expected the algorithm to find the inverse of the known transformations. The displacement fields were created with the following formula:

$$\mathbf{u}(\mathbf{x}) = \begin{pmatrix} c_1 + c_2 \cdot \sin(x_1) \\ c_1 + c_3 \cdot \cos(x_2) \end{pmatrix}, \quad (5)$$

c_1 , c_2 , and c_3 being normally distributed numbers with zero mean and standard deviations 8, 5 and 5 respectively. Results

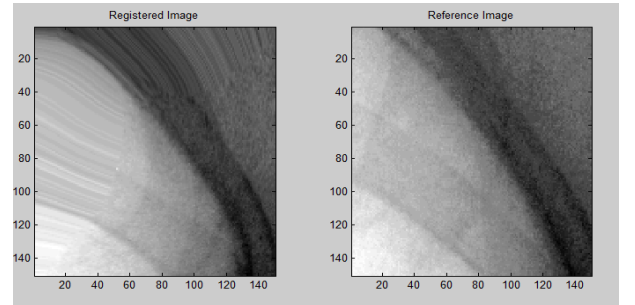


Figure 3. A case of unhandled unsatisfactory primary registration. The compensated rigid transformation was not large enough, and secondary registration tried to compensate the remaining translation, expanding the pixels on the side of the image.

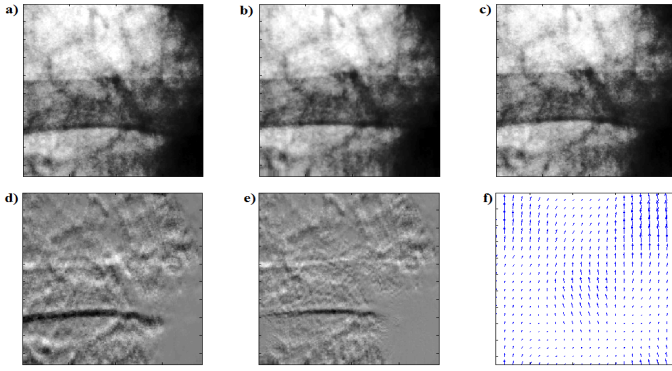


Figure 4. Results of the DTCWT based registration algorithm in a synthetic test: **a)** study before registration; **b)** study after registration; **c)** template; **d)** difference before registration; **e)** difference after registration; **f)** resulting displacement field

indicate, as shown in table I, that segmentation of the images can improve run times. Since the quality of the registration is already satisfactory at $\Delta \mathbf{u}$ values of 2.5-3, a 256×256 pixels resolution represents a good compromise between precision and speed, and was chosen to be the standard of the algorithm.

B. Comparison with Demons

In order to objectively evaluate the effectiveness of the algorithm, we chose to implement a well-known registration algorithm as a basis for comparison. Demons algorithm is an extensively studied and verified registration algorithm proven to be fast and accurate in most cases [13].

The results of the implemented algorithm compared to the wavelet-based method are depicted on Figure 5. As it is to be seen, Demons registers the two images with a minimal remaining error, finding a smooth displacement field between them. The wavelet-based method solves the registration problem as well, similarly decreasing the difference between the images. As expected, the DWT based method registered only low-frequency components on the right side of the study, leaving the high frequency differences on the left side unregistered.

Based on these results, we can conclude that the wavelet-based method has the potential to solve the contralateral subtraction problem.

Table I. Effectiveness of the registration algorithm for different ROI sizes¹.

ROI size (pixels)	$\bar{t}_{run}$ (sec)	Mean ROI number per lung	T_{run} (sec)	$\Delta \mathbf{u}$ (pixels)
64×64	0,50	190	95	4,04
96×96	0,84	90	75,6	3,7
128×128	1,01	51	51,51	3,0
192×192	1,84	27	49,68	2,36
256×256	2,92	16,0	46,72	2,58
384×384	7,77	7,4	57,5	1,96
512×512	11,09	5,5	61	1,58

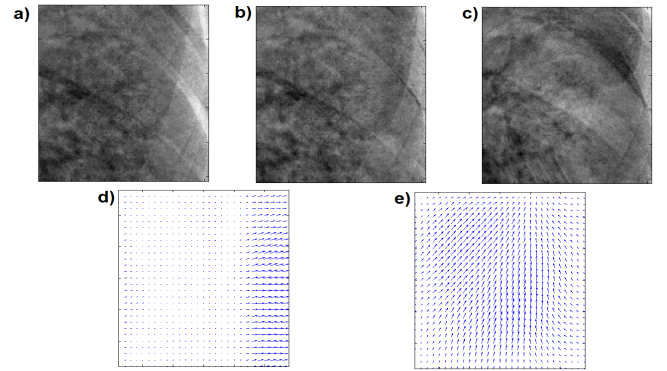


Figure 5. Results of the two algorithms on a pair of images after primary registration: **a)** difference before registration; **b)** difference after registration with DWT; **c)** difference after registration with Demons; **d)** displacement field after registration with DWT; **e)** displacement field after registration with Demons.

C. Verification

Ultimately, the aim of the verification is to assess to what extent the proposed c-sub scheme helps the diagnostic process. This can be done with the help of a radiologist, as done by Kawaguchi et al. [3], or as used e.g. by Yoshida [14], by comparing the effectiveness of a nodule detector with and without symmetry analysis, expecting a reduction of false positives. We used the latter approach, with a nodule detector that is part of a complex CAD system, in which the symmetry analyzer has been integrated.

The results of the contralateral subtraction are used for false positive elimination in the following way. On the output of the nodule detector, four features describing symmetry are calculated for each result candidate. Then a support vector machine classifier is used to filter the results, ideally eliminating symmetric false positive findings, while keeping asymmetric objects including true nodules.

The four features in essence calculate the contrast of a segmented nodule candidate compared to its surroundings on the difference image. A high (positive) value is expected when the contrast of the structure is higher than the contrast of the same structure in the contralateral region. The first three features calculate respectively the minimum, maximum and average values inside the automatically segmented nodule and in its surrounding area, and take the difference for the two areas. The fourth feature uses a circle of variable radius instead of the nodule border when calculating the averages, to reduce error when nodule segmentation fails.

Figure 6 shows the resulting Receiver Operating Characteristic (ROC) curve on the output of the classifier using

¹The notations of table I:

$\bar{t}_{run}$: mean run time on one ROI,

T_{run} : estimated complete run time: $T_{run} = \sum_{ROI_s} \bar{t}_{run}$,

$\Delta \mathbf{u}$: mean deviation, i. e. the mean of norms of the difference vectors between the applied and calculated $\mathbf{u}$ displacement fields.

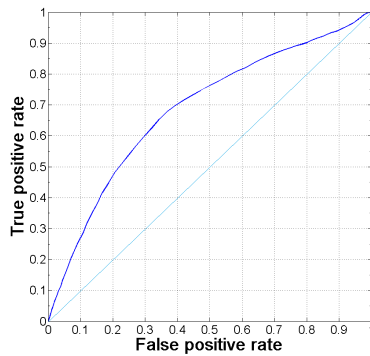


Figure 6. ROC curve on the output of the classifier using the described features

10-fold cross-validation of 247 chest images from the JSRT public database [15]. The area under the ROC curve (AUC) is 0.6944 using an optimistic estimate, and 0.6782 using a pessimistic one. These values mean that some false positives could be eliminated at a cost of losing a smaller fraction of true positives. Although these results are not outstanding, they clearly indicate the potential of the c-sub scheme.

Figure 7 shows the resulting Free-Response Operator Characteristic (FROC) curve of the complete CAD system on the same image set with and without symmetry analysis. The results show, that the sensitivity of the system improves considering the same number of false positives as in the case without contralateral subtraction. With the usage of the proposed symmetry-analysis the average sensitivity improvement of the CAD-system is 6.6% on the depicted relevant interval.

V. CONCLUSION

Based on the above results the proposed DTCWT based registration method is able to emphasize asymmetrical information on chest radiographs. Registering low-frequency wavelet components as a means of regularization seems to be a valid concept, as we demonstrated in several tests. Synthetic tests showed basic functionality of the approach, as well as effectiveness comparable with a well-known and proven

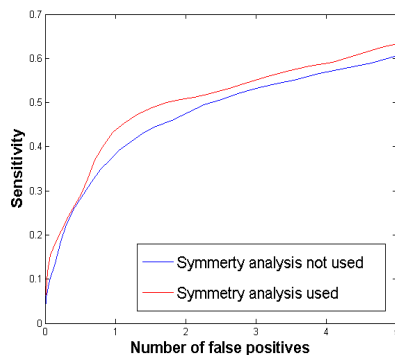


Figure 7. FROC curve on the output with and without using the features provided by symmetry analysis

registration algorithm. Having integrated our current methods with a CAD system for nodule detection, we have verified that the nodule detection sensitivity of the system has improved while maintaining the same number of false positives.

ACKNOWLEDGMENT

The research discussed above is partly supported by the grant TÁMOP - 4.2.2.B-10/1-2010-0009.

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