Digital image subtraction of temporally sequential chest images for detection of interval change

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An automated digital image subtraction technique for temporally sequential chest images has been developed in order to aid radiologists in the detection of interval changes. A number of small regions of interest (ROIs) are selected automatically in the lung areas of two temporally sequential chest images. A local matching, based on a cross-correlation method, is performed on each pair of corresponding ROIs in order to determine shift values for the coordinates of two images. A proper warping of \(x,y\) coordinates is obtained by fitting two-dimensional polynomials to the distributions of shift values. One of the images is warped and then subtracted from the other. Forty six pairs of chest images (42 with interval changes and 4 without interval change) were processed using this method. The subtraction images were able to enhance various important interval changes, such as differences in the size of tumor masses, changes in heart size, and changes in pulmonary infiltrates or pleural effusions. Approximately 70% of the pairs showed reasonably good registration.

Key words: subtraction, chest radiography, interval change, image registration, nonlinear geometric warping

I. INTRODUCTION

In clinical practice, chest radiographs are commonly interpreted in comparison with previous radiographs of the same patient. At the University of Chicago Hospitals, approximately 80% of chest radiographs are interpreted side by side with previous radiographs of the same patient. Such comparison readings help radiologists to identify abnormalities and to determine their clinical significance. They are also important in detecting interval changes in known abnormal findings, so that the effect of treatment can be evaluated properly. However, it is reported that important interval changes can be missed by radiologists even when they observe serial chest radiographs.

In this study, we investigated the application of digital image subtraction techniques to temporally sequential posteroanterior (PA) chest images in order to enhance interval changes and alert radiologists, thereby improving their diagnostic accuracy.

Investigators have reported that digital image subtraction techniques can potentially provide clinically useful information related to interval changes in chest images. However, difficulties of image registration have not yet been adequately solved. A subtraction image derived from a pair of temporally sequential chest images would have a uniform zero value except for regions with interval changes, if the two images had been produced in an identical manner. However, clinical chest radiographs are not usually reproducible in terms of patient positioning, x-ray projection, inspiration, and cardiac pulsation as well as pathology. Therefore, a proper image registration technique is needed prior to the subtraction, so that a pixel on one image can be subtracted from one corresponding to the identical normal anatomic structure on the other image.

II. METHODS

A. Analysis of misregistration

Initially, we studied 59 pairs of temporally sequential PA chest images that had been selected randomly, and classified the causes of radiographic misregistration into four types, namely, lung expansion, lateral inclination, AP inclination and rotation. Shift of the patient body parallel to the film plane is excluded from the causes. Figure 1 illustrates the four types of misregistration and the frequencies of their incidences per pair of chest images. Some cases had misregistration due to a combination of two causes, which resulted in the total frequencies exceeding 100%. The frequency of misregistration due to at least one of the causes was 86% (51) for the 59 cases studied. It is apparent from Fig. 1 that radiographic misregistration is generally complicated since radiographs correspond to two-dimensional projections of three-dimensional objects. Therefore, a nonlinear distortion (warping) of one of the images relative to the other would be required to obtain an accurate registration.

B. Transformation of image coordinates

Nonlinear geometric warping of \(x,y\) coordinates has been utilized in change detections of radar images, aerial photographs, and satellite photographs. In this article, we present a method for nonlinear geometric warping. We assume that Cartesian coordinates of two images are given by \((x,y)\) and \((x',y')\). A transformation between \((x,y)\) and
\[(x', y')\] can be represented by using shift values \(\Delta x\) and \(\Delta y\), and two-dimensional polynomials of an appropriate order, as given by
\[
x' = x + \Delta x, \\
y' = y + \Delta y, \\
\Delta x = \sum_{i=0}^{n} \sum_{j=0}^{n-i} a_{ij} x^i y^j, \\
\Delta y = \sum_{i=0}^{n} \sum_{j=0}^{n-i} b_{ij} x^i y^j,
\]
where \(n\) indicates the order of polynomials, and \(a_{ij}\) and \(b_{ij}\) are coefficients.

We assume here that a current chest image is distorted (or warped) due to one of the projection variables and is expressed by \((x', y')\). A previous chest image may be assumed nondistorted and is expressed by \((x, y)\). Then the pixel value at \((x + \Delta x, y + \Delta y)\) on the current image corresponds to the pixel value at \((x, y)\) on the previous image. The "warping" (or rewarping) of the current image is required for subtraction with the previous image (see details of coordinate transformation in Appendix).

Shift values \(\Delta x\) and \(\Delta y\) can be determined for a given set of \(x\) and \(y\), using a local template matching technique\(^9\),\(^10\) as illustrated in Fig. 2. A template on the left in Fig. 2 corresponds to a small region of interest (ROI), which is centered at \((x, y)\) selected in one image. A search area on the right corresponds to a large ROI selected in the other image, where the "best match" subregion \(B_{x', y'}(i, j)\), centered at \((x', y')\), is searched for producing the greatest similarity to the template \(A(i, j)\). \(\Delta x\) and \(\Delta y\) are then derived from \((x, y)\) and \((x', y')\), using Eq. (1).

**C. Overall scheme**

The digital chest images used in this study were obtained by digitizing conventional screen-film chest radiographs (Kodak OC film with Lanex Medium screens) using a Konica Laser Film Scanner KFDR-S with a matrix size of 2000 × 2000 and a 10 bit gray scale. The digitized images were subsampled to a 500 × 500 matrix with an effective pixel size of 0.7 × 0.7 mm\(^2\), because abnormalities in chest images which are subjected to our subtraction study are generally very large, as will be demonstrated later. First, a nonlinear density correction is performed in order to adjust the density and contrast in the two digitized images. Ribcage edges are detected based on analysis of image profiles. A number of template ROIs and the corresponding search area ROIs are then selected in the lung areas on the two images for local matchings. Shift values \(\Delta x\) and \(\Delta y\) are then derived by the local matching technique on each pair of ROIs. A two-dimensional curve fitting is performed on the set of mapped shift values, \(\Delta x\) and \(\Delta y\), in order to determine a proper warping of \(x, y\) coordinates of one image. The warped image is then subtracted from the other image. The analysis was performed on a DEC VAXStation 3500 computer.

1. **Nonlinear density correction**

A nonlinear density correction technique based on the H and D curve of the original radiographic films\(^11\) is applied as a preprocessing. With this technique, the "proper" density distributions can be recovered from improperly exposed radiographs, and thus consistent density and contrast in temporally sequential chest images can be maintained. An exposure correction factor is estimated based on histogram analysis of a chest image. A proper look-up table for the correction factor is chosen from several look-up tables for density correction of the improperly exposed radiographs. Details of this technique are described elsewhere.\(^11\)

2. **Selection of template ROIs and search area ROIs**

Ribcage edges are detected based on analysis of the first and second derivatives of profiles through chest images. The outline of detected ribcage edges is then fitted to a polynomial curve, as described in detail elsewhere.\(^12\),\(^13\) The template ROIs and the corresponding search area ROIs are automatically located entirely within the lung regions (including the mediastinum) of the two images, which are identified by the outlines of ribcage and diaphragm edges. The distance between the centers of the two adjacent ROIs is 16 pixels. Template ROIs are 32 × 32 pixels in size and search area ROIs are 64 × 64 pixels in size. The template ROIs are positioned first in the lung region of a previous
chest image, and then the centers of search areas on a current chest image are located by globally shifting the centers of the template ROIs, namely, search center coordinates = template center coordinates + global shift. The amount of this shift is equal to the shift between the locations, in two chest images, of the crossing of the midline of the chest with the top of the lungs.

3. Local matching based on cross-correlation method

We employed a cross-correlation method for the local matching technique. The “best” match subregion $B_{x'y'}$ is obtained when the normalized cross-correlation value with template $A$ becomes the maximum. The matrix size for $A$ and $B_{x'y'}$ is $I \times J$. The normalized cross-correlation value $C_{x'y'}$ is given by

$$C_{x'y'} = \frac{1}{IJ} \sum_{j=1}^{J} \sum_{i=1}^{I} \frac{\{ A(i,j) - \bar{a} \} \{ B_{x'y'}(i,j) - \bar{b} \}}{\sigma_a \sigma_b},$$

where

\[ \bar{a} = \frac{1}{IJ} \sum_{j=1}^{J} \sum_{i=1}^{I} A(i,j), \quad \sigma^2_a = \frac{1}{IJ} \sum_{j=1}^{J} \sum_{i=1}^{I} \{ A(i,j) - \bar{a} \}^2, \]

\[ \bar{b} = \frac{1}{IJ} \sum_{j=1}^{J} \sum_{i=1}^{I} B_{x'y'}(i,j), \]

\[ \sigma^2_b = \frac{1}{IJ} \sum_{j=1}^{J} \sum_{i=1}^{I} \{ B_{x'y'}(i,j) - \bar{b} \}^2. \]

Note that $C_{x'y'} = 1$, if subregion $A$ and subregion $B_{x'y'}$ are identical. Shift values of $\Delta x$ and $\Delta y$ for the best match are then derived by using Eq. (1) for each pair of ROIs.

4. Determination of nonlinear warping of $x$, $y$-coordinates

Figures 3(a) and 3(b) indicate the distributions of shift values $\Delta x$ and $\Delta y$, respectively, derived for all the centers of template ROIs over the image for a particular pair of digital chest radiographs. The regions outside the lung are not subjected to the local matching technique and thus have zero values in these distribution plots. A two-dimensional curve fitting with 10th order polynomials, based on a least-square method performed in order to obtain the coefficients $a_{ij}$ and $b_{ij}$ in Eq. (2). The distributions of fitted shift values are shown in Figs. 4(a) and 4(b). Shift values for the pixels outside the lung region are
determined by linear extrapolations of those inside the lung area, and thus $\Delta x$ and $\Delta y$ for all pixels in a chest image can be obtained. The current chest image is then warped based on the fitted shift values. The pixel value at $(x,y)$ on the warped image corresponds to that at $(x + \Delta x, y + \Delta y)$ on the original current image, which is calculated by a linear interpolation method as described earlier.

5. Subtraction

A subtraction image is obtained by the difference between the warped current image and the previous image.

In this study, we subtract the former from the latter, and add a certain offset value to display the image with positive pixel values. After the contrast is enhanced by a factor of 1.6 using a “windowing” technique, subtraction images were printed on 8 in. $\times$ 10 in. films using a Konica Laser Film Printer KFDR-P. Figures 5(a)–5(d) illustrate a pair of original chest images without significant interval change, the warped image, and the resulting subtraction image. In the subtraction image obtained with this nonlinear registration technique, normal anatomic structures such as ribs and vessels are removed and the whole lung region seems
relatively uniform because of accurate registration. Note that the edges of the film (warped image) are distorted due to the complicated transformation. However, another subtraction image, shown in Fig. 5(c), which was obtained by simply shifting one of the images relative to the other, indicates significant artifacts due to mismatch of normal anatomic structures. This result clearly indicates the need of a nonlinear warping technique for accurate registration of temporally sequential chest images.

III. RESULTS

We tested our method on 46 pairs of temporally sequential chest images which consisted of 42 pairs with interval changes due to various abnormalities and 4 pairs without interval change. Original radiographs were selected by a chest radiologist. The selected cases contained all of the four types of misregistration illustrated in Fig. 1. However, image pairs involving extremely severe misregistration were excluded in this study.

Figure 6 shows a pair of temporally sequential chest images with interval changes and the subtraction image obtained with this method. The subtraction image greatly enhanced a new focal air-space infiltrate in the right upper lobe and three subtle metastatic nodules (arrows). The horizontal white artifact in the lower left lung indicates the change in the diaphragm level.

Figure 7 shows another pair of images with a subtle nodule and the subtraction image. It is very difficult to detect this subtle lesion due to overlap with the right clavicle and a rib. The interval change was, however, more conspicuous on the subtraction image due to removal of bone shadows. It is also apparent that the subtraction image has potential to increase an observer’s confidence that there has been no clinically significant interval change in the other regions.

Another case with multiple lesions is shown in Fig. 8, where a number of tumor nodules are unchanged, but the size of a large mass in the mediastinum has slightly decreased due to therapy. The subtraction image clearly indicates the amount of change in the mass. The image registration was not completely successful for this pair, since artifacts due to the mismatch of normal anatomic structures are observed in the left lung region.

It was found that the subtraction images were able to enhance the conspicuity of various types of interval change, such as (1) change in pulmonary infiltrates, (2) change in the size of tumor masses, (3) change in pleural...
effusions, (4) change in heart size, (5) change in air fluid levels, (6) change in the size of pneumothorax.

IV. DISCUSSION

In order to investigate the extent of correlations between temporally sequential chest images, we examined the distributions of the normalized cross-correlation values obtained in local matchings. Figure 9 illustrates locations of templates with small cross-correlation values (less than 0.7) in a pair of chest images. In this case, the correlation value was small around the venous access catheter over the right upper lobe in one of the images, and also around interstitial infiltrates and a nodule with interval changes in the left lower lobe. It was found that poor correlation was generally obtained around regions which were difficult to match, because of (1) large lesions with interval changes, (2) location changes of devices, (3) interval changes in the borders of the heart or diaphragm, (4) changes in the locations and angles of clavicles, and (5) regions with extremely low density. These regions tend to give unusually large or small shift values, as observed in some areas in Figs. 3(a) and 3(b). Incorrect shift values due to such "poor matching" are not useful and can even disturb proper fittings for correct shift values which may exist near the poor matching region. Therefore, we attempted a weighted fitting method on the shift values, such that shift values with large cross-correlation values are given large weights in the fitting based on a look-up table as shown in Fig. 10. This method was generally very effective in improving local registration around the poorly matching regions.

Accuracy of the image registration technique including the weighted fitting method was subjectively evaluated by a chest radiologist using the 46 cases. Subjective judgment of the matching/mismatch was based on the obviousness of mismatch artifacts which tend to show a pair of black and white shadows. Approximately 70% (32) of all the cases examined showed "reasonably" good matchings, indicating no apparent mismatch for normal anatomic structures. An additional 15% (7) were considered acceptable, although they contained some mismatches in parts of the lungs. Another 15% (7) indicated apparent mismatches which may be due to lateral inclination, rotation, or a failure in detecting ribcage edges. Note that these results may not be applicable to a large group of nonselective clinical chest images.

We studied the effect of the size of the square template ROIs. Figure 11 shows the relationship between the average normalized cross-correlation value and the CPU time as the template size is varied. Template sizes smaller than
24×24 produced many “poor matching” shift values and thus small average cross-correlation values, although the CPU time was small. However, the CPU time increased as the template size increased. The results in Fig. 11 indicate that a template size of about 32×32 pixels (22.4×22.4 mm²) is appropriate for practical use, when the cross-correlation method is used.

The poor performance with small template sizes can be explained by the fact that the average distance between posterior rib edges in chest images is approximately 20 mm. Templates smaller than this distance are more likely to produce local matching errors because they may not contain rib edges, which are major structures in the thorax. If a part of the rib is included in a template, the local matching becomes more accurate. A large size template also may not be appropriate. Even if a large template can provide a proper matching for the entire area of the large ROI, it does not necessarily produce the “best” match for the central area of the ROI. Therefore, the shift values obtained using the large ROI may be incorrect. However, we did not find a significant error in the registration even with the largest template size (64×64 pixels) employed in this study.

The preliminary results obtained with our method appear to be encouraging. However, in order to apply this method for practical use in routine clinical work, it is desirable to improve the accuracy of the image registration technique. As described earlier, major causes of failure in image registration are due to (1) substantial lateral inclination, (2) substantial rotation, and (3) incorrect ribcage detection due to the presence of gross abnormalities. Both (1) and (2) resulted in incorrect selection of search area ROIs, such that some search areas did not include the same structures as those in the corresponding templates. This wrong selection of search area ROIs was caused by the global shift method used in this study. These results indicate that our method for selection of ROIs needs to be improved to cover a larger area.

It should be noted that misregistrations caused by large amount of difference in x-ray projection, such as severe AP inclination or rotation, could not be completely accommodated with this method. Developments of devices which can make patient positioning more reproducible are highly desirable in order to take advantage of the digital image subtraction technique. Although the current processing time of our method (approximately 12 min/image pair) is relatively long, it can be reduced by using a faster computer and by optimizing the software. One important advantage of our automated method is that it can be easily implemented in the context of a digital imaging environ-
ment, such as a PACS (Picture Archiving and Communica-
tion System) which will become available in the future.

V. CONCLUSION

A digital image subtraction technique for temporally sequential chest images is presented based on an automated image registration technique using a nonlinear geometric warping prior to the subtraction. The conspicuity of various types of interval changes was enhanced in the resulting subtraction images. We believe that this technique can be developed into a new computer-aided diagnostic scheme in chest radiography.15

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APPENDIX: TRANSFORMATION (WARPING) OF IMAGE AND OBJECT COORDINATES

Figure 12(a) illustrates a warping of chest image-1 in order to obtain proper registration between two chest images. Here, chest image-1 and chest image-2 correspond to the current and the previous chest image, respectively. Suppose anatomic structure at a pixel located at \((x, y)\) on image-1 corresponds to the pixel at \((x + \Delta x, y + \Delta y)\) on image-2. A proper warping of image-1 is then required to move the pixel at \((x, y)\) to \((x + \Delta x, y + \Delta y)\), which results in a transformation of the square grid pattern on the upper left to the distorted grid pattern shown on the upper right. It should be noted that the square grid patterns in Fig. 12(a) indicate coordinates for images on film. However, if we apply grid patterns which indicate coordinates for ob-
FIG. 12. Registration of two chest images using a nonlinear warping in two different coordinates systems applied to (a) images on film and (b) objects or anatomical structures.

jects, this transformation can be illustrated in a different way as shown in Fig. 12(b). The distorted grid pattern on image-1 in Fig. 12(b) indicates the distortion of the object (or anatomical structures), such that the pixel value at \((x + \Delta x, y + \Delta y)\) on image-1 corresponds to the pixel value at \((x, y)\) on image-2. The "warping" (or rewarping) of image-1 is now required for a transformation of the distorted grid pattern on the upper left to the square grid pattern on the upper right in Fig. 12(b).

These two methods (a) and (b) appear to be conceptually different; however, they will produce the same result if the distance increment in the grid patterns is very small, or if in practice the pixel size is much smaller than \(\Delta x\) and \(\Delta y\). Our method in this study is based on method (b), since the calculations of pixel values on the warped image are simpler than those for (a). The pixel value at \((x, y)\) on the warped image-1 with method (b) should be equal to that of \((x + \Delta x, y + \Delta y)\) on the original image, which can be calculated by interpolation of pixel values at four adjacent pixels near \((x + \Delta x, y + \Delta y)\) on the original image-1, if \(\Delta x\) and \(\Delta y\) are not integers. With method (a), however, the pixel value of the warped image-1 at a pixel location of \((x + \Delta x, y + \Delta y)\) is given by the pixel value of the original image-1 at \((x, y)\). Since the pixel cannot be located at \((x + \Delta x, y + \Delta y)\) unless \(\Delta x\) and \(\Delta y\) are integers, the warped image-1 must be constructed by calculating the estimated pixel values at proper locations on the Cartesian coordinates, which requires somewhat more complicated interpolation.