Non-rigid image registration for temporal subtraction of whole-body nuclear medicine images

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***Abstract*— A non-rigid registration algorithm for application to whole-body emission images of the same patient is presented. Rigid registration is generally insufficient to properly register whole-body images, a certain amount of deformation needs to be applied to obtain a good correspondence. This deformation should not change the size or shape of lesions, bones and the general anatomy. In our approach, non-rigid registration is accomplished by maximisation of mutual information, and regularised by a weighted least squares deformation constraint. Maximisation of mutual information I is accomplished by a preconditioned iterative gradient ascend algorithm using an analytically exact expression for the gradient of I with respect to individual pixel displacements. Anatomy is taken into account by parameterising the constraint according to a simple thresholding segmentation so as to allow large deformations in air, small in soft tissue and no deformation in bone or lesion tissue. A pyramidal multi-resolution approach is used to speed up the registration process. The performance of the method was evaluated by registering deformed phantom images, initial tests on 2D whole-body clinical images also show promising results.**

I. Introduction

NUCLEAR emission imaging methods (SPECT and PET) show great advantages in detecting specific lesions and tracking their evolution during the course of treatment. Subtraction of images acquired before and after treatment is useful to facilitate detection, quantification and tracking of lesions, provided that the images have been properly aligned or registered. To obtain a proper correspondence on whole-body scans it is necessary that this registration allows a non-rigid deformation, but it should also retain the proper anatomy of the patient and not change the size or aspect of lesions.

Many non-rigid registration methods already exist. The non-rigid deformation can be represented using smooth basis function [1] or constrained by an elastic, viscous-fluid or other regulariser [2]. In general however these methods do not take the underlying anatomy into account, and it is difficult to limit the deformations of certain regions of interest (e.g. lesions). We propose a non-rigid registration algorithm based on the maximisation of the mutual information I between the source (reference) and target (floating) image, that is based on exact calculation of the gradient of I with respect to individual pixel displacements [3]. The minimisation of a weighted sum L_c of square length differences in each pixel serves as a regularising constraint. The weights are adjusted according to segmented anatomical details in the images. Iterative gradient ascend is then used to find the combined optimum of $(I - \beta L_c)$, where β is the weight of the constraint. The algorithm is vastly speeded up by employing a multi-resolution scheme.

This work was supported by F.W.O. grant G.0174.03. All authors are with K.U.Leuven. (e-mail: raf.claessens@uz.kuleuven.ac.be)

II. Method

Mutual information is a measure from the field of information theory that has shown to be an excellent similarity measure for image registration. For two images, it is a measure of how well one image explains the other and vice versa.

The calculation of mutual information I is based on the joint histogram of grey values in both images, it is given by:

$$I = \sum_{a,b} \frac{h_{ab}}{N} \ln \frac{N h_{ab}}{h_a h_b}$$

where h_{ab} is the joint histogram (distribution) of grey values a in the reference image r and grey values b in the floating image f, h_a and h_b are the marginal histograms and N is the sum of all histogram entries. Since misregistration increases the dispersion of the joint histogram, one can see that registration is achieved for the most crisp histogram possible.

The joint histogram h_{ab} is computed using partial volume interpolation [4], such that h_{ab} and I are continuous and almost everywhere differentiable functions of the displacement field. The local gradient of I is used as a driving force toward a registered image. The coordinates of each pixel in the floating image are updated proportionally to the driving gradient. The gradient of I in pixel (x_j, y_j) with respect to x_j is given by:

$$\frac{dI}{dx_j} = \sum_{a,b} \frac{dI}{dh_{ab}} \frac{dh_{ab}}{dx_j} = \sum_{a,b} \frac{1}{N} \left(\ln \frac{N h_{ab}}{h_a h_b} - I \right) \frac{dh_{ab}}{dx_j}$$

$\frac{dh_{ab}}{dx_j}$ is itself a (very sparse) histogram with the same dimensions as h_{ab} and can be calculated efficiently using partial volume interpolation.

The diagonal elements of the Hessian matrix of I are used to determine a pixel-dependent step size to speed up the gradient ascend.

As the gradient of I deforms the floating image g only due to the grey level features present in both images, features that are not present in the reference image f and uniform regions of constant greyscale will not move at all. Hence, we want to design a constraint that should regularise the gradient of I. It should strive to conserve the topology of the image, allow translation and rotation but resist large local deformations. The constraint we used is simply a weighted least squares sum of the change in distance from each pixel to its neighbour pixels. The constraining cost L_c for pixel (x_j, y_j) in the kth iteration

step is defined as:

$$L_{cj}^{k} = \sum_{i=0}^{n} w_{i,j} \left(L_{i,j}^{0} - L_{i,j}^{k} \right)^2$$

where $L_{i,j}^{0}$ is the initial distance from the current pixel j to its ith neighbour, $L_{i,j}^{k}$ is the deformed distance and $w_{i,j}$ is the corresponding weight. The weights $w_{i,j}$ form a window for the square differences. This window should at least include all 8 adjacent pixels (in 2D) if the constraint is to conserve the topology. Since the constraint is then only propagated by 1 pixel per iteration, convergence can be speeded up by the additional inclusion of some distant pixels in the window.

The first derivative of L_c can be readily calculated, the second derivative of the constraint can be approximated as $\sum w_i$ and the inverse is used as a (fixed) stepsize.

A crude segmentation is done by smoothing and thresholding to distinguish between air and (dense) tissue. The constraint weights are adjusted to allow for a greater deformation in air, and only a small deformation in dense tissue.

For large deformations between the target and the source image, the pixel-based gradient of I is very small. The rate of convergence is greatly improved by using a multiresolution scheme, while maintaining the accuracy of the method.

III. Results

An example of the application of the algorithm to clinical images is shown in figures 1 and 2. Figure 1 shows an example of a follow-up ^{99m}Tc-MDP bone scan of a patient with prostate cancer. In the initial scan on the left we see multiple bone metastasis in the axial skeleton. During follow-up, disease progression is seen in the right pelvic bone (middle image). The subtraction image on the right does not show clear features due to misregistration of both images. In the subtraction of the initial scan and the registered follow-up scan in figure 2, the progressive lesion is immediately recognisable and almost no skeletal features are visible anymore, indicating a good registration.

IV. Discussion

We proposed a simple discrete algorithm based on the maximisation of mutual information and a constraining energy term that conserves anatomy while allowing translation, rotation and global deformations. A tissue-dependency was introduced in this constraint. While computationally more expensive than methods based on radial basis functions or on an elastic filter kernel, deformation in regions of interest can be restricted and anatomy can easily be taken into account. The algorithm can be efficiently implemented, the computation time for large 2D images is acceptable (in the order of 5 mins. for the 1024x256 example images). Our current research includes the extension of the algorithm to 3D images for application in PET-oncology (PET-PET follow-up studies and PET-CT studies of the same patient). Also, an extended segmentation for modalities offering greater anatomical detail will be examined, for instance segmentation of bone in CT images, or of the PET transmission scan.

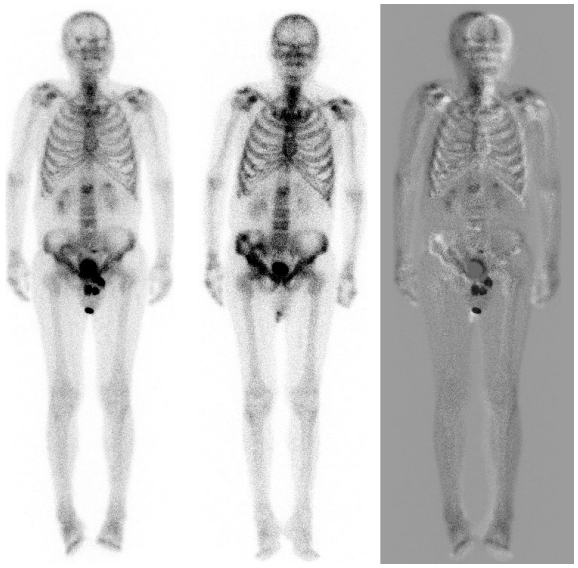

Fig. 1. Left to right: Reference image, unregistered floating image and subtraction of the two images.

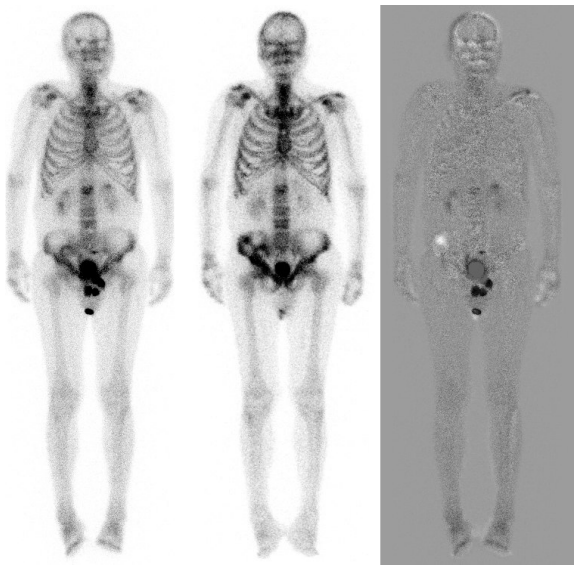

Fig. 2. Reference image and registered floating image. A progressive lesion in the pelvic bone is clearly highlighted in the subtraction.

References

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