Comparison of three methods used for fusion of SPECT-CT images of liver metastases

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Abstract-*We compare three methods for fusing SPECT-CT images: ImageMatch - an automatic three-dimensional/two-dimensional method developed by Focus Imaging; IBM Visualization Data Explorer - a three-dimensional interactive method developed by International Business Machines, Inc.; and qsh - an interactive three-dimensional/two-dimensional method developed at New York University. While many fusion methods have proved successful for registering brain images, most methods have been less successful for thoracic and abdominal images. We use images of liver metastases obtained with a radiolabeled breast tumor-directed antibody to illustrate the strengths and weaknesses of the methods reviewed. The images used are typical clinical images from eight patients. We conclude that an optimal image fusion program should combine the strengths of each of the methods reviewed.*

Key words: image fusion, methods comparison, image fusion validation, SPECT-CT fusion, clinical use of image fusion, metastatic liver cancer.

1 Introduction

Recent advances in tomographic functional imaging techniques such as Single Photon Emission Computed

Tomography (SPECT) and Positron Emission Tomography (PET), that involve radiolabeled substances such as anti-tumor antibodies or tumor receptor ligands have proven extremely useful and accurate in the diagnosis of tumors. In particular, the use of these radiolabeled substances to detect abnormal concentrations of tumor associated antigens in metastatic sites has increased.[1,2] X-ray imaging modalities that give structural details, such as Computed Tomography (CT) or non-radiation imaging techniques such as Magnetic Resonance Imaging (MRI) and UltraSound (US), cannot, at present provide the functional information provided by SPECT or PET scans.

Radiation oncology treatment planning and evaluation, as well as the diagnosis of cancer, are frequently accomplished using images obtained in several different ways. The structural imaging methods such as CT, US, and MRI, provide exquisite anatomic detail, and in many instances, can help the physician localize abnormal masses or enlargement of lymph nodes.[3] Difficulties in interpreting these images occur where enlargement of lymph nodes or abnormal bulk of tissue may not represent tumor. Determining which masses represent cancer requires visualizing their function - their activity. Functional imaging methods such as SPECT, PET, or magnetic resonance spectroscopy (MRS) provide physiological parameters such as metabolic rate, tumor antigen concentration or chemical content, but often are lacking in anatomical landmarks which would allow precise localization of the observed areas of abnormal radiopharmaceutical accumulation or the identification of the metabolically active portion of a tumor, thus making treatment difficult. In this particular study we matched functional SPECT images with anatomic CT images. In other work we have matched many other image combinations. All three of the methods we contrast in this study are capable of matching any pair of images, i.e., functional-functional, structural-structural or functional-structural.

There is a vast literature, particularly in recent years, describing attempts to perform image registration, both automatically and semi-automatically, mainly in the head. Several good review articles,[4,5,6] give incite into the problems and to many proposed solutions. Additionally, there is a great deal of emphasis on sub-millimeter accuracy which might be necessary for neurosurgery, but is not necessary for cancer diagnosis and treatment and not attainable with functional images which have a pixel size great than one millimeter. The contribution of the work performed in our laboratory is that it applies anywhere in the body, does not need fiducial markers, hence is retrospective, and can employ native measurement techniques. Even registration methods and algorithms which claim to be fully automatic actually incorporate a mechanism for user interaction[7] or require preprocessing.[8] One difficulty that most attempts at image registration share, is the difficulties encountered in attempting image registration in areas of the body other than the head.[9.10]

While the use of SPECT has increased the sensitivity of the detection of abnormal concentrations of tumor associated antigen using radiolabeled antibodies[11], the problems associated with SPECT images are several-fold. SPECT images provide very little anatomical detail; it is often nearly impossible to determine the transaxial level of a particular SPECT slice. Thus the normal landmarks used in evaluating SPECT images may not be easily identifiable. It is difficult to determine the structure in which there is an abnormal localization of antibodies. In addition it may be difficult to identify

structures in which there is normal uptake of the radiopharmaceutical. This provides difficulty in the staging of tumors and in surgical planning. In addition, the persistence of activity in blood pool can obscure the diagnosis or diagnostic finding. There may also be non-specific interactions between the radiopharmaceutical and normal tissue that may be difficult to differentiate from specific interactions with the tumor. Certain organs show persistent activity as well. The kidney and sometimes the hepatobiliary system accumulate radioactivity due to their role in the clearance of the radiopharmaceutical. SPECT scans can help distinguish between blood vessels and abnormal lymph node uptake.[12]

The difficulties associated with CT are ones of interpretation. Abnormal masses cannot be identified positively as tumors; they can represent fibrosis from a prior surgery or therapy or other benign entities; alteration or distortion of normal anatomy by surgery or prior disease. Certain landmarks are unreliable or are masked by the variable positioning of structures such as loops of small bowel. Lymph nodes cannot be considered abnormal until they measure more than one centimeter. Sometimes this may lead to a false negative distinction which leads to improper staging. False negative results would occur when a hyperplastic lymph node was considered abnormal. CT scans cannot differentiate between an inflamed or hyperplastic lymph node and a metastatic tumor.[13]

However, SPECT and CT used together can distinguish benign from malignant growths. Post-operatively they can be used to distinguish scar tissue from regrowth of tumor. This is particularly helpful in the thorax and abdomen where there is more variation of organs and tissues than in the head. Image registration thus has applications in cancer diagnosis and staging, surgical planning, and radionuclidic therapy as well as in radiation treatment planning.[14,15]

2 Methods

For this study we used a cohort of 8 patients with advanced breast cancer who were participating in a study for the evaluation of the In-111 radiolabeled epithelial mucin-specific huBrE-3 antibody. The first two SPECT image sets were acquired on a three-headed gamma camera (Trionix Research Laboratories Inc.). These instruments produce an image which has a cubic voxel 3.56 mm on each side and a matrix size of 128x128x2 bytes. The remaining cases were acquired on a dual-headed gamma camera (Toshiba America Medical Systems). These instruments produce an image which has a cubic voxel 4.3 mm on each side and a matrix size of 128x128x2 bytes. In each case, a total of 120 projection slices are reconstructed into 60 to 70 image slices covering the field of view.

All CT scans were performed on one of two scanners (GE HighLight Advantage or GE High Speed, both from General Electric Medical Systems, Milwaukee, WI). Oral and/ or a bolus injection of contrast medium (Conray 43; Mallinkrodt, St. Louis, MO) followed by intravenous infusion, were administered. Between thirty and fifty transaxial sections were acquired each into a 512x512x2 byte matrix having a voxel size of 7.0 mm x 0.654297 mm x 0.654297 mm. CT slices were intentionally acquired with a slice thickness near a multiple of the slice thickness of the SPECT images.

Images were transferred by our hospital ethernet (TCP/IP) network to a common computer system (HP 9000/ C180V48, Hewlett Packard Company, Palo Alto, CA) and converted to a common,

standard image format (Interfile[16]). Appropriate software modules were written so that this format could be utilized by all three of the fusion methods.

The first fusion method used, Image Match, is an automatic method developed by Focus Imaging. The images are reformatted in three dimensions but are only viewable in two dimensions as coronal, sagittal and axial slices. All three projections are shown in the same image panel. After each image is entered into the program and numerous parameters are chosen, the images are matched automatically. The algorithm used to actually do the matching consists of characterizing the pixel values in terms of potential energy and then minimizing this energy field. The images are then rotated and translated to bring them into alignment. The resulting fused data set is displayed as dithered SPECT-CT images in the three orthogonal planes so that one can appreciate and evaluate the details of the registration.

The second fusion method used, known as IBM Visualization Data Explorer (DX), is a software suite which provides an object-oriented, graphical programming interface. The DX data model is discipline-independent (i.e., it can be used for any visualization application including medicine), self-describing, and supports regular and irregular grids with node and connection-dependent data. DX uses a data-flow driven client-server execution model. The method of image fusion is interactive. Data Explorer allows the extraction of volumes or of one or more isosurfaces from each image set. Slices in one of the three orthogonal planes (coronal, sagittal, axial) from either or both image sets, may be overlaid on the three dimensional image. Additionally, contours at selected levels from either study may be similarly overlaid. Furthermore, slices in any projection may be viewed simultaneously with isocontours overlaid in a separate image window.[17] The three dimensional surfaces together with the two dimensional slices are then visually matched. The two three-dimensional isosurfaces to be matched, are overlaid at all times including the final match. The resulting transformed images are displayed as fused three-dimensional isosurfaces using different colors and different degrees of transparency.

Both of the methods described above offer, at present, only rigid body transformations to accomplish the fusion. For the thorax and abdomen, it is often advantageous to use a warping technique such as a polynomial or elastic fit. Both methods are currently being extended to implement warping algorithms.

The third fusion method which is part of an image display and processing toolkit known as qsh, uses an interactive non-rigid, polynomial transformation method to fuse the images. Although the three dimensional image sets are manipulated, qsh is capable of displaying images only in two-dimensions. The fusion method used by qsh is a two step process. The first step, after displaying corresponding axial, coronal and sagittal slices with appropriate color scales, consists in choosing suitable rotation angles after which an oblique transformation[18] is performed on one of the image sets to render the slices from it co-planar with the slices in the other image set. In the second step, between ten and twenty-five landmark pairs (ten to fifteen pairs for first order and fifteen to twenty-five pairs for second order polynomial warping) are then chosen on selected slice pairs. Linear regression analysis is performed on the landmarks, followed by a Gauss Jordan matrix inversion to find the eigenvalues of the matrix which form the transformation coefficients[19]. Either first or second order polynomials are used, depending on the severity of the transformation. The warping coefficients, the

eigenvalues, are then used together with a resampling technique to determine the new coordinates for each pixel in the image to be moved. The alteration achieved by the application of the algorithm may be performed on either the images themselves or on a region of interest (ROI) which describes an outline of a structure on the CT or MRI or a concentration of radioactivity on the SPECT. If one image set is transformed into the other image set, slices from the two matched image sets can be viewed overlaid in different color scales and with different degrees of transparency. This method was developed at NYU and has had extensive validation of the matching results.[20]

3 Results

Using all 3 methods, we were able, with varying degrees of difficulty to achieve a match. ImageMatch required prior extraction of the liver image from the CT. The automatic algorithm associated with ImageMatch then produced an estimate that the matching of the CT with the SPECT image was within 87-98%. The resultant fused image as displayed were not always consistent with the estimated match results. Figure 1 illustrates a very acceptable match on patient number six. The time to achieve the match is very short, on the order of a few minutes, once the image parameters were entered into the program. However, the necessity of segmenting the CT liver by hand added a considerable amount of time to the process. Also, as there were no facilities in ImageMatch itself to accomplish the necessary interactive segmentation, we used the image processing programs available in qsh

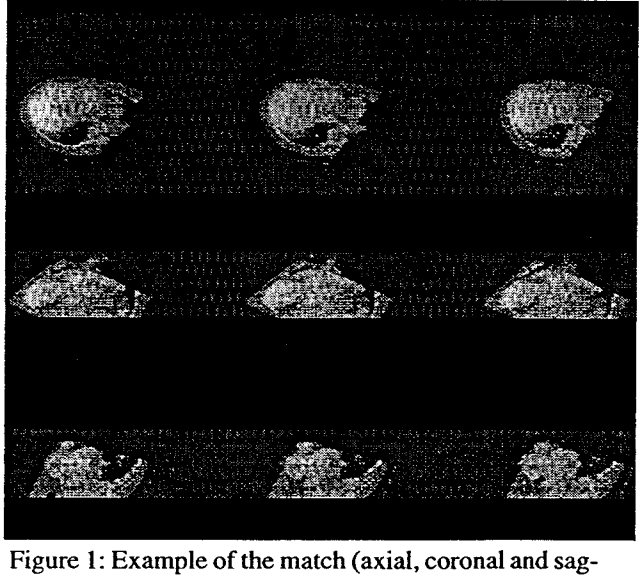

Figure 1: Example of the match (axial, coronal and sagittal slices) as displayed by ImageMatch.

Neither Data Explorer nor qsh required any special image preparation. Quantitative assessment using patients with/ without stereotactic frames,[21] suggests that using visualization alone, DX can match image sets within 5.8±2.9 mm. Figure 2 illustrates the type of match that can be obtained with DX.

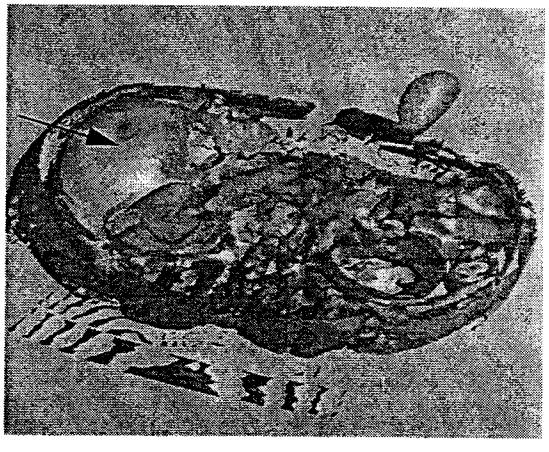

Figure 2: Example of the match achieved using IBM Visualization Data Explorer (DX). Note the small liver nodule visualized in upper left of the image.

Qsh, as formerly validated,[20] has been shown to match within 1.3 SPECT pixels. In Figure 3 we illustrate the match obtained with qsh by overlaying the ROIs drawn on the CT image on the SPECT image. It should also be noted that DX and qsh work with the full 2 byte data set. Both DX and qsh take on average, one half hour to achieve a satisfactory match and require that the operator have some skill.

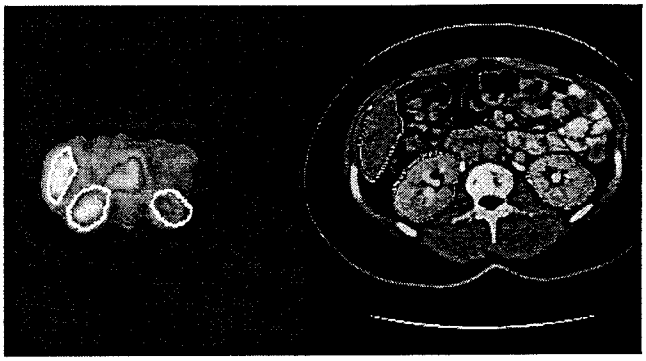

Figure 3: Example of a match achieved using qsh.

4 Discussion

Qsh permitted generation of region of interest ratios for liver, blood pool and tumor. Although confidence in the accuracy was greater for the larger structures, i.e. liver, it was the only program with this feature. While ImageMatch allows greater registration speed, it has less resolution and requires pre-processing of the images in some circumstances such as matching in the abdomen. DX offers better visualization both globally and locally. Only qsh allowed semiquantitative analysis. DX, on the other hand, offers better visualization of both global and local structures, but requires a more highly trained user.

5 Conclusions

The main purpose of this study was to evaluate image registration software in the context of specific clinical applications. It was concluded that the optimal program should combine the speed of ImageMatch, the visualization of DX and the semi-quantitative analysis of qsh. It was also found that it is of clinical value to understand the different types of image registration displays - two dimensional versus three-dimensional visualization. Furthermore, it is worthwhile to appreciate and learn how to circumvent the difficulties encountered when using fully automatic registration methods in the abdomen and to identify the usefulness of semi-quantitative analysis. The correct identification of radiolabeled tumor antibody uptake in both normal and abnormal liver tissue can be very efficacious in the management of cancer patients.

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7 References

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