MEDICAL IMAGE REGISTRATION: BASIC SCIENCE AND CLINICAL IMPLICATIONS

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Image Registration is a process of aligning two or more images so that corresponding feature can be related objectively. Integration of corresponding and complementary information from various images has become an important area of computation in medical imaging. Merging different images of the same patient taken by different modalities or acquired at different times is quite useful in interpreting lower resolution functional images, such as those provided by nuclear medicine, in determining spatial relationships of structures seen in different modalities. This will help in planning surgery and longitudinal follow up. The aim of this article was to introduce image registration to all those who are working in field of medical sciences in general and medical doctors in particular; and indicate how and where this specialty is moving to provide better health care services.

Keywords: Medical imaging, Image processing, Image registration, Image fusion, Hybrid imaging, Automation, Robotic medical intervention

INTRODUCTION

Diagnostic imaging has gained a pivotal role in the health care system. From its primitive shape to present gigantic status, the imaging modalities have gone through progressive and fast development both in vertical and horizontal directions.[1] Availability of simple X-ray imager could not be guaranteed in early 70 even at district hospital level in many countries of the word and now hybrid systems like PET-CT and SPECT-CT are functioning to provide a combined look of anatomy and physiology.[2]

Different diagnostic imaging modalities provide a wide spectrum of diverse information about the body structures and functions. Conventionally different images are evaluated by diagnosticians as separate diagnostic files and then information are combined to reach any final diagnosis. Image registration, which is basically aligning of two or more images, if applied intelligently in the diagnostic departments then all the information from all imaging modalities can be combined together at pixel level. This can make the use of resources more efficiently and effectively.[3]

Diagnostic imaging as a subject gets very little consideration in undergraduate curriculum.[4] Image registration, a sub-discipline logically cannot get any better place in conventional teaching system. This neglected field like many other modern sciences are not properly understood even at postgraduate level in developing countries. Postgraduate radiology and nuclear medicine curriculum/programs do not address this subject to any extent. This article is to review the basic science of image registration for medical professionals. Published literature is also reviewed to summarise the present status of image registration in medical sciences.

DEFINITIONS AND METHODS

Image Registration can be defined as a process of aligning two or more images so that corresponding feature can be related objectively. Recently process of alignment is extended to computer models, atlas and even physical space which have paved way for robotics and automation in medicine and surgery.[5]

Pre-requisites of image registration: Reference image, target image and a transformation model are the basic and utmost required components of image registration. Reference image is the image which is taken as standard and all subsequent images are manipulated (by the process of image registration) to look like this standard image.[6] Most of the time, in intra-subject image registration, patient's own first/baseline image is taken as reference image. This is done in longitudinal follow-up cases. In all other cases where inter-subject registration is necessary like as in biomedical research or applying statistical models on a group of subjects then either one subject is taken as standard or a mean image is generated first which will serve as standard in all future manipulations. Atlas is used if patient's image is compared with pre-defined data such as Talairach atlas.[7]

Target image is the image which is to be manipulated to look like reference image. Certain mathematical operation is done on this image so that it is aligned to standard image/atlas with reasonable accuracy and more importantly to keep the inherent difference in intact form. Transformation matrix is calculated through multistage iteration. Transformation matrix is applied to target image and data is projected to form legible display.[8] It can be simplified as following:

Let us assume image A as reference and image B as target image.

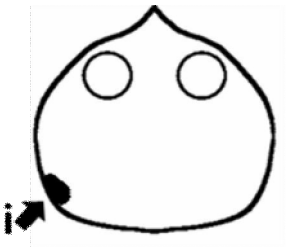


Image A with Spot i

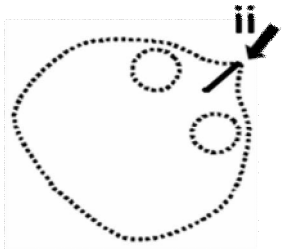


Image B with line ii

Figure-1: Reference and target images

Image B is located at different coordinates compared to image A and an important feature line (ii) is there in the image. Image A contains a special feature of black spot designated (i). Comparing the two images:

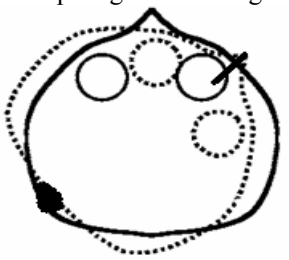


Figure-2: Image B superimposed on image A for transformation matrix

Transformation matrix 'T (x,y,z)' generated and applied resulting:

Figure-3: Transformed image B, resulted a new image C

Image 'C' is similar to size, shape and coordinates that of image A but contains all vital information inherent in image B. So mathematically this process will be represented as:

$$A(j,k) = C(j,k) + d(j,k)$$

$$C(j,k) = T(x,y,z) \otimes B(j,k)$$

Calculation of transformation matrix involves multiple iteration and comparison of reference image with resultant image (at each step). This determines certain predefined parameter (called Cost Factor). Optimisation of cost factor will determine the termination point of iteration and reaching the final stage.[9,10]

Let us consider two digital image data set each consisting of 4 pixels with digital value surrounded by pixels containing background signals (assuming value 1 each). Image data set A is reference and B is target.

1	1	1	1		1	1	1	1	1	1
1	**12**	**13**	1		1	1	1	1	1	1
1	**13**	**12**	1		1	1	1	1	1	1
1	1	1	1		1	1	**23**	**25**	1	1
					1	1	**24**	**24**	1	1
					1	1	1	1	1	1
					1	1	1	1	1	1
					1	1	1	1	1	1
					1	1	1	1	1	1
		A						B		

Image B is located in different x,y coordinates. Transformation model will calculate ratio of corresponding pixels and that will be as follows:

1	1	1	1	0	0
1	12	13	1	0	0
1	13	12	1	0	0
1	1	**0.043**	**0.04**	0	0
0	0	**0**	**0**	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0

Value in each box (representing pixel) is ratio of corresponding box in image A divided by that of image B. These values are used to compute mean and standard deviation. Mean of ratio=1.251 and standard deviation=3.45. Cost factor=mean of ratio/standard deviation and is equal to 2.76.

Now after each step of data shifting all the calculation are repeated till an optimum cost factor is reached and does not further improve with more iterations. At this final stage data is re-sliced and displayed as registered image.

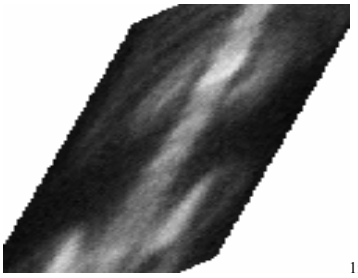
Now let us apply this to real life example. Consider a spot view of bone scan of the same patient taken by two different systems and displayed under two different protocols.

Image A

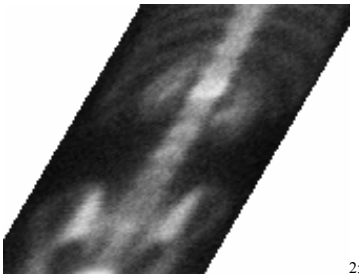
Image B

Figure-4: Image before registration

Although both scans contain identical information regarding diagnosis of this patient but due to difference in display/acquisition it is nearly impossible to compare them directly. It may require heavy mental exercise of an expert diagnostician to extract some useful information for comparison. Image registration of this data set will involve following 5 steps:



1: Rotation 30 degree clockwise



2: Skewed 30 degree vertically

3: 30 degree skewed horizontally

4: Colour scale inverted, Final image B

5: Image A

Figure-5: Step 1 to step 5 of image registration

In this case after fifth step of colour scale inversion, image B becomes similar to image A.

RESULTS OF PUBLISHED LITERATURE

Pubmed was searched for the terms 'medical image registration', 'image registration', 'review/meta analysis of image registration', relevant paper published in English language and papers with title word image registration from database till October 2009.

A total of 4107 papers/reports were listed on Pubmed, among them 3893 papers are in English literature. Papers with title word image registration are 259 and 182 are review papers. Distribution of published papers based on use of image registration for diagnosis or therapy is depicted in Figure-6.

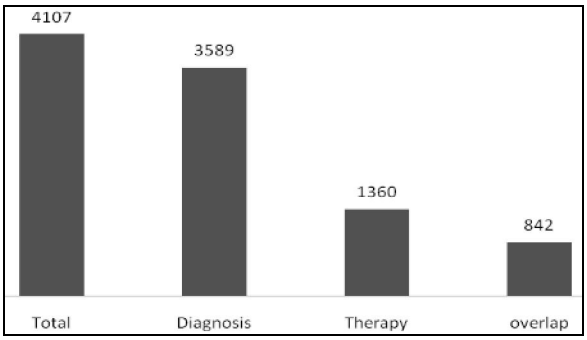


Figure-6: The published literature about image registration and its application in medical sciences (October 2009)

Papers published in the decades 1991–2000 and 2001–2009 is shown in Figure-7.

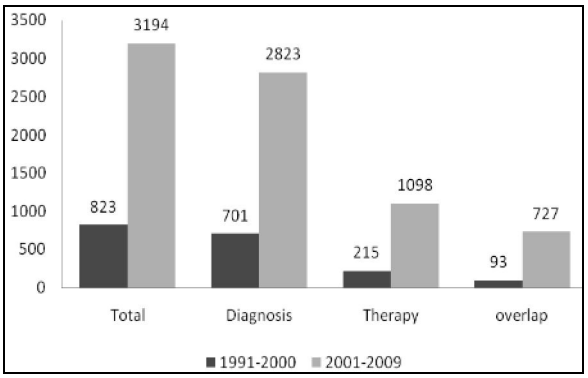


Figure-7: The published literature about image registration and its application in medical sciences in two successive decades (search completed till 31st October 2009)

DISCUSSION AND CLINICAL IMPLICATIONS

Medical image registration has many applications both in diagnostics and therapeutics.[11] Although it has penetrated into biomedical research in addition to clinical application yet its mainstay remained in radiological imaging. Diagnosticians if not using image registration have to fuse information various image information mentally and have to mentally compensate for any changes in subject position for longitudinal follow up. Image registration provides an easy way to fuse information from various modalities with different aspects of information about the pathophysiological processes.[12] Image registration is quite important in many aspects like correct delineation of lesions (Figure-8).

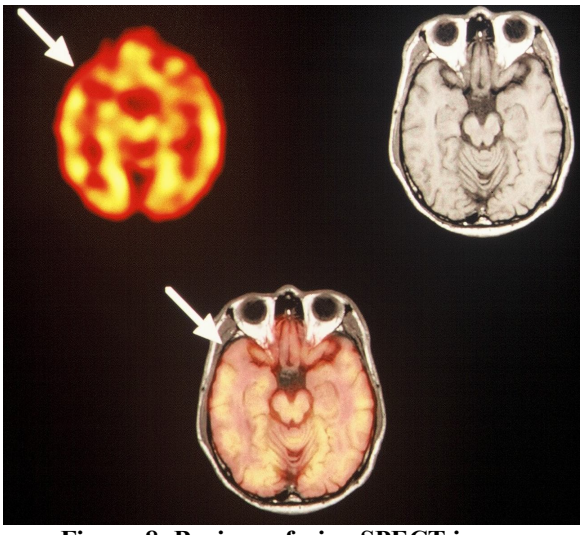


Figure-8: Brain perfusion SPECT image registered with respect to corresponding high resolution anatomical image.

Fusion of images can delineate the correct size and localisation of epileptogenic focus. This helped in surgical removal of whole of the focus and patient was cured.

Image registration can assist in aligning multiple image of same subject (intrasubject registration)[13] and also helps to compare images acquired form different subjects (intersubject registration). This later process is essential for application of any mathematical/statistical model on digital data. Figure-9 shows an example of mean image generation.[14] Voxel based variance or comparison of variance can also be depicted as shown in Figure-10.[15]

Statistical models can be applied on pixel by pixel of digital data of experimental models (Figure-11). Medical images are treated as matrices in mathematics and point by point objective analyses are done with various parameters and confounding factors. Based on statistical exclusion, even abnormal areas can delineated. Computer can analyse the medical images if these are in digital format and are registered to any standard template. Automated reporting is possible and this is an important step towards bringing artificial intelligence in medicine (Figure-12). This is also helpful in training junior doctors in diagnostic imaging specialties. Report generated by such automated system might guide doctors to make up mind for final manual reports.[16]

Most modern use of image registration is guided intervention.[17,18] X-ray film guided surgery was actually the first application of medical image registration. A patient with a broken needle in the hand was diagnosed and successful surgery was done in Birmingham, UK in December 1895, just two months after the introduction of X-ray. This fact is actually illustrated in Figure-13 (upper right quadrant).

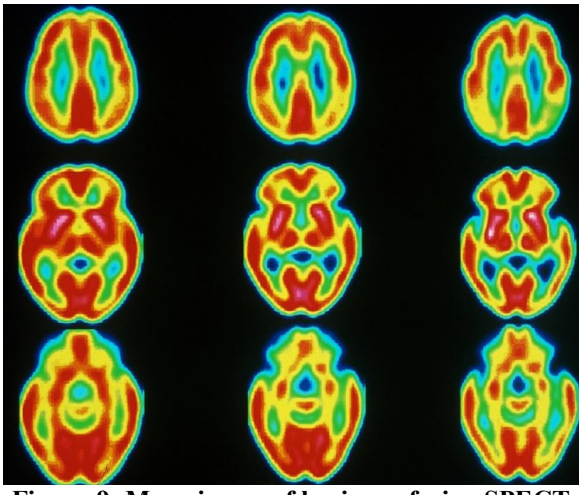


Figure-9: Mean image of brain perfusion SPECT scans of 18 normal subjects, voxel based computation done.

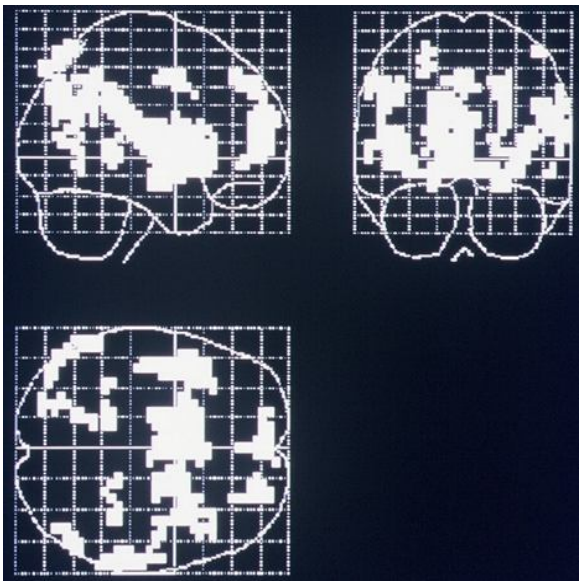


Figure-10: Voxel based computation of variance in point by point data (voxel values) of brain SPECT scans on group of subjects, results displayed on glass brain after image registration on a standard template.

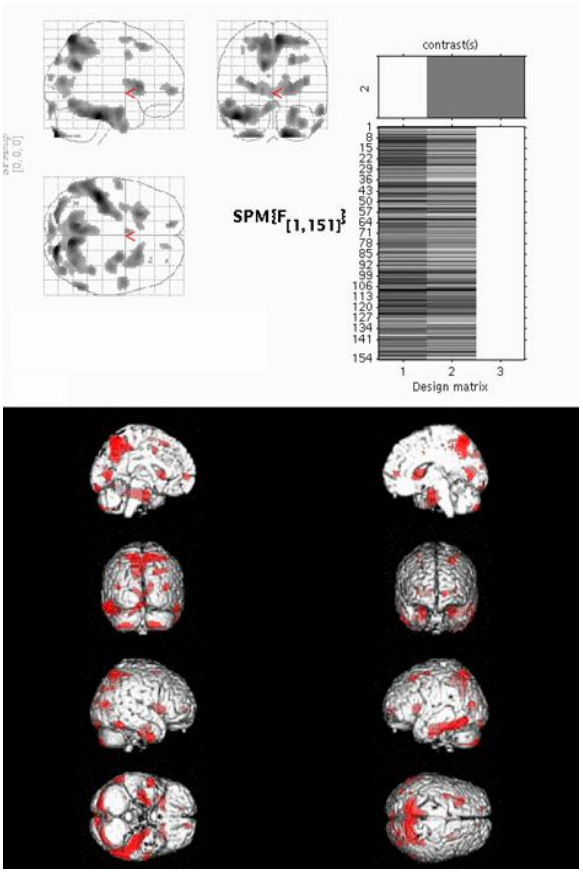


Figure-11: Statistical model applied on brain images of 151 subject and results displayed on standard brain.

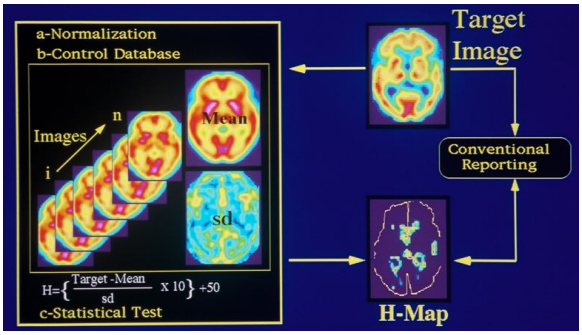


Figure-12: A step towards automated evaluation of medical imaging data

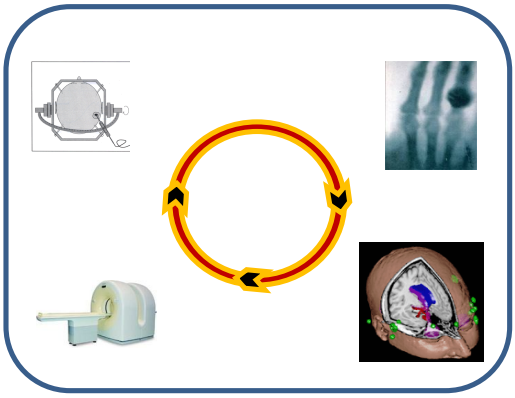


Figure-13: Life history of image registration and its future prospects.

Data shown graphically in Figure-6 and 7 indicate that there were strong efforts to bring image registration in the main stream of medicine. There was exponential growth of literature in the current decade (Figure-7) indicating accelerated result oriented efforts in the field of image registration. Paper published in the period January 2001 to October 2009 are 4–5 fold compared to those published in last decade (1991–2000). Importance of image registration and fusion provided stimulus for industry to bring the hybrid imaging system.[19] These are installed throughout the world and have a strong impact in patient management system.

Scientists working in the field of image registration are now pushing hard to automate diagnostics and therapeutics. Guided stereotactic intervention is becoming popular. Fixation of rigid frame followed by imaging and then intervention is mastered at many centres in the world. Ultimate goal of such efforts is definitely complete automation. The process will move towards online registration of images to physical space and interfacing computation devices to guide intervening surgical instruments for guided surgical operations.[20,21] Fast technological advancements, fast computation and minimisation of size of instruments are bringing hopes in near future.

CONCLUSION

Medical image registration is an important sub-speciality with lots of research and application potentials. Medical doctors and medical physicists should be trained at-least to have basic know-how of the field. In future this field will be very important because it is moving towards automated intervention.

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