Application Of Joint Intensity Algorithms To The Registration Of Emission Tomography And Anatomical Images

by

Yiu Hon LAU

A thesis
submitted for the Degree of
Doctor of Philosophy

University of Technology, Sydney

July 2004

CERTIFICATE OF AUTHORSHIP / ORIGINALITY

I certify that this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

Signature of Candidate

Production Note:
Signature removed prior to publication.

Acknowledgement

I would like to express my grateful appreciation to Prof. Michael Braun and Prof. Brian F. Hutton who have touched my life by offering their support and assistance to make this thesis possible. They were the driving force in keeping me going when I almost gave up the study. They encouraged me in my area of research and inspired me to submit papers for local and international conferences. There is no doubt that they contributed considerably to the readability and content of this thesis, for which I wish to thank them. I recall the memorable workshop we attended together at Utrecht in Netherlands. They motivated me and made me feel that my work was valued. Prof. Braun introduced me to relevant digital image processing algorithms, and aspects of CT and MR physics. His experience in the field, his many ideas and suggestions have been extremely valuable and instructive. Prof. Hutton introduced me to image reconstruction techniques, the MCAT phantom, IDL programming language and gamma camera physics. What I learnt about SPET cameras, their operation, data acquisition and processing has proved to be of great benefit to this study. Prof. Hutton's expertise in nuclear medicine together with his leadership was invaluable to the research group at the Westmead Hospital. I appreciate the supportive and friendly atmosphere in the group, enhancing scientific interaction among us. Discussions with my supervisors helped me to keep both feet on the ground, which was not always easy.

Special thanks are due to my colleague, Mr. David Skerrett. It has been a privilege to know and work with him over the past few years. He is a senior medical physicist with a special talent in computer networks. He taught me much about UNIX. With his assistance, my life in the computer laboratory was made easier. He also gave me support in the use of software applications, UNIX workstations, networks, MO disks and drives, FTP and emails… and he generously gave of his personal time. I enjoyed talking with him especially when we walked together to the car park after a day of hard work. He kindly proofread the entire thesis. I wish him all the best.

Acknowledgment is also due Dr. Leighton Barnden, Chief Medical Physicist at the Department of Nuclear Medicine of Queen Elizabeth Hospital in Adelaide for providing me with advice on my registration software. He supplied clinical data for validation of the automatic retrospective multimodality image registration package *MIR*. I also thank

Dr. Lennart Thurfjell, then of Uppsala University, for the enlightening discussion about image registration during his visit to Sydney. He gave me the inspiration for the implementation of the registration algorithm. Thanks also to Dr. D.K. Chung and Dr. R. Howman-Giles of the Department of Nuclear Medicine at the Children's Hospital at Westmead in Sydney for critically evaluating *MIR* in clinical practice. They have offered me the clinical data and the opportunity to perform this research.

I thank Rochelle Hatton and Seu Som for invaluable discussions and for the enjoyable atmosphere that made the research pleasant and productive. It was a great pleasure to work with them. I also wish to thank Dr. George Larcos, Dr. David Farlow, Dr. Simon Gruenewald, Dr. Kevin Choong, Dr. Lee Collins and Mr. George Bonovas for supporting this research at the Westmead Hospital. I also wish to acknowledge the contributions of Mr. Erin McKay at St. George Hospital, Sydney for providing SPET and CT images, Dr. S. Meikle at the Royal Prince Alfred Hospital, Sydney, for providing the OSEM reconstruction source code, and Dr. George Zubal of Yale University for providing the Zubal phantom. I acknowledge the financial support provided by the Australian government via the Australian Postgraduate Award as well as the Department of Medical Physics, the Westmead Hospital, and the Department of Applied Physics, University of Technology, Sydney, for assistance with conference expenses.

Finally, from the bottom of my heart, I thank my "better half", Carol, who was always there to support me, along with my kids: Eppie and Anisa. Without their support it would not have been possible for me to finish this study.

The work reported in this dissertation was carried out in the Department of Applied Physics at the University of Technology in Sydney, and the Department of Medical Physics & Department of Nuclear Medicine and Ultrasound at Westmead Hospital in Sydney.

Table of contents

List of acronyms and mathematical symbols by chapter

Chapter 1

2D	two dimensional
3D	three dimensional
CT	computerized tomography
MR	magnetic resonance
NMR	nuclear magnetic resonance
SPET	single photon emission tomography
PET	positron emission tomography
PACS	picture archiving and communication system
μ	linear attenuation coefficient
$\mathbf{M}$	macroscopic magnetization
$\mathbf{M}_{xy}$	transverse magnetization
$\mathbf{M}_{Z}$	axial magnetization
$\mathbf{B}$	magnetic field
T_1	longitudinal relaxation time / spin-lattice relaxation time
T_2	transverse relaxation time / spin-spin relaxation time
PD	proton density
γ	gyromagnetic ratio
ω_o	larmor frequency
RF	radio frequency
G	magnetic field gradient
FDG	^{18}F-fluoro-deoxyglucose

Chapter 2

fMR	functional MR
$\mathbf{Q}$	4×4 matrix representing a rigid-body transformation in homogeneous coordinates
$\mathbf{Q}'$	3×3 rigid-body transformation matrix
$\mathbf{T}$	4×4 translational matrix in homogeneous coordinates
$\mathbf{R}$	4×4 rotational matrix in homogeneous coordinates
$\mathbf{S}$	4×4 scaling matrix in homogeneous coordinates
$\mathbf{I}$	Identity transformation
$\mathbf{R}'$	3×3 orthonormal rotation matrix
$\mathbf{t}$	3-element translation vector (t_x, t_y, t_z)
φ	3-element rotation vector (φ_x, φ_y, φ_z)
$\mathbf{S}'$	3-element scale vector (s_x, s_y, s_z)
$\bar{y}$, $\bar{x}$	centroid of $\{y_i\}$ and $\{x_i\}$
SVD	singular-value decomposition
$\mathbf{Q}^T$	transpose of a matrix Q
$\mathbf{D}$	diagonal matrix
$\mathbf{U}$, $\mathbf{V}$	orthonormal matrices
$\lVert x - y \rVert$	Euclidean distance between x and y

SAD	sum of the absolute differences
SSD	sum of squared differences
$\overline{\mathrm{A}}$	mean intensity in image A
N	number of voxels in the overlapping image volume
F	number of fiducial markers
PV	partial volume interpolation
Φ	similarity measure
M	number of intensity bins
FRE	fiducial registration error
TRE	target registration error

Chapter 3

A	floating image to be aligned with the reference image
A′	transformed floating image (unless otherwise indicated, this image is interpolated and sampled in the domain of the reference image)
B	reference image
x	voxel position expressed in homogeneous coordinates
$a = \mathrm{A}(x)$	voxel intensity of image A at x
$b = \mathrm{B}(x)$	voxel intensity of image B at x
$\tilde{\Omega}_A$	continuous domain (“field of view”) of image A
Ω_A	discrete image domain of A: $\Omega_A \subset \tilde{\Omega}_A$
Ω_{AB}	discrete overlap of image domains of A′ and B, $\Omega_{AB} = (\tilde{\Omega}_{A'} \cap \tilde{\Omega}_B) \cap \Omega_B$
S_b	a subimage of A′ induced by b in B such that $\mathrm{S}_b = \{x \in \Omega_{AB} : \mathrm{B}(x) = b\}$
T	a mapping of A to A′ that includes interpolation
T_θ	a mapping parameterized by transformation parameters θ
θ	a vector of registration parameters $(\varphi_x, \varphi_y, \varphi_z, t_x, t_y, t_z)$
$\mathrm{T}_\theta\mathrm{A}$	transformed image A′
PDF	probability density function
Q	matrix representing a spatial transformation of voxel coordinates, $x' = \mathbf{Q}x$
$\mathrm{A}(\mathbf{Q}x)$	transformed image A′ such that $\mathrm{A}'(x) = \mathrm{T}_\theta\mathrm{A}(x) = \mathrm{A}(\mathbf{Q}\,x)$
x'	location of voxel x transformed by **Q**: $x' = \mathbf{Q}x$
$\mathrm{P}(a)$	probability density function of intensity in image A
$\mathrm{P}(b)$	probability density function of intensity in image B
(a,b)	intensity pair of a joint intensity histogram of images A and B, where a belongs to the range of A and b belongs to the range of B
$\mathrm{P}(a,b)$	joint probability of A and B
$\mathrm{P}(a\|b)$	conditional probability of A given B
H(A)	entropy of an image A
H(A,B)	joint entropy of images A and B
H(A|B)	conditional joint entropy of image A given the knowledge of B
MI(A,B)	mutual information of images A and B
NMI(A,B)	normalized mutual information of images A and B

μ_A	mean intensity of image A
μ_b	mean intensity of a subimage S_b
$\sigma^2(a)$	variance of intensity of image A
$\sigma^2(a \mid b)$	conditional variance of intensity of a subimage S_b given b in B
CR(A,B)	correlation ratio of A and B
SCR(A,B)	symmetric correlation ratio of A and B

Chapter 4

$[n_1,n_2,n_3\|M]$	downsampling of the transformed floating image $T_\theta A$ and the reference image B by a factor of n_1 in the x-direction, n_2 in the y-direction and n_3 in the z-direction, and M is the number of bins in the intensity histogram
^{99m}Tc-HMPAO	technetium-99m hexamethyl-propylene amine oxime (HMPAO)
DE	displacement error measures the average Euclidean displacement over all eight vertices of a bounding box
FLE	fiducial location error

Chapter 5

PMT	photomultiplier tube
NaI (Tl)	sodium iodide crystal doped with about 0.5% of thallium oxide
PHA	pulse height analyzer
PSF	point-spread function
FWHM	full width at half maximum
d	path length in an attenuating medium
$f(x,y)$	radioactivity distribution in Cartesian coordinates
$\hat{f}(x,y)$	estimated radioactivity distribution
FBP	filtered back projection reconstruction
$g(s,\theta)$	slice profile (projection) is defined as the total count detected in a time interval at pixel s from the origin when the detector is at an angular position θ
p	total number of projections
MLEM	maximum likelihood expectation maximization reconstruction
OSEM	ordered Subsets Expectation Maximization reconstruction
N_θ, N	number of projection angles and number of bins per projection
$\boldsymbol{A}$	transition matrix such that $g = \boldsymbol{A}f$
g_i	number of counts in the i^{th} measurement
α, β	collimator constant and collimator scale of a given gamma camera
d	source-detector distance
σ	Gaussian width $\sigma = \alpha + \beta \times d$ used to estimate the PSF of a gamma detector

Chapter 6

θ	rigid body transformation, $\theta(x) = \mathbf{R}x + \mathbf{t}$
$\mathbf{R}$, $\mathbf{t}$	rotational and translational misalignment
θ_{app}	applied transformation

θ_{rec}	recovered transformation
ε	registration error
ε_R	rotational error, $\varepsilon_{\text{R}} = \frac{1}{8}\sum_{i=1}^{8}\left\|(\mathbf{R}_{\text{app}} - \mathbf{R}_{\text{rec}})\, x_{\text{i}}\right\|$
ε_t	translation error, $\varepsilon_{\text{t}} = \left\|\mathbf{t}_{\text{app}} - \mathbf{t}_{\text{rec}}\right\|$
$\bar{\varepsilon}$	mean registration error
AC	attenuation correction
SD	standard deviation

Chapter 7

SSD	sum of squared differences of voxel values between images
$u(x)$	displacement vector at x
$\tilde{u}$	measured displacement vector
T_u	transformation T parameterized by a displacement vector field u
$\text{T}_u\text{A}(x)$	floating image A transformed with respect to a *reference* image B using transformation T parameterized by a displacement vector $u(x)$ where x is the position vector in the reference image such that $\text{A}'(x) = \text{T}_u\text{A}(x) = \text{A}(x - u(x))$
$\sigma_b{}^2$	conditional variance indexed by b
σ^2	variance of A′
i	image voxel index $i \in \{0, 1,..., \text{N-1}\}$
j	grid nodes index j
ϕ	Gaussian kernal $\phi\left(x_{ij}\right) = \exp\left(-\tfrac{1}{2}\left\|x_{ij}\right\|^2 / \delta^2\right)$
δ	Gaussian width
$\left\|x_{ij}\right\|$	Euclidean norm of $\left\|x_i - x_j\right\|$ on R^3
$\left(\text{c}_j\right)$	column vector consisting of n coefficients corresponding to n grid nodes such that $u(x_i) = \sum_{j\in Q}\phi\left(x_{ij}\right)c\left(x_j\right)$
$\left(\phi_{j'j}\right)$	$n \times n$ matrix of Gaussian weights $\phi_{j'j}$
v	residual displacement vector field obtained by convolution $v\left(x_i\right) = \phi\left(x_i\right) * \tilde{v}\left(x_i\right)$
ε	displacement error given by $\varepsilon_i = \left\|u_i - \tilde{u}_i\right\|$
DE	RMS displacement error
ADE	average RMS displacement error

Chapter 8

ε	displacement error given by $\varepsilon_i = \left\|u_i - \tilde{u}_i\right\|$
DE	RMS displacement error
ADE	average RMS displacement error over all images

List of illustrations

List of tables

Appendix

Abstract

In current practice, it is common in medical diagnosis or treatment monitoring for a patient to require multiple examinations using different imaging techniques. Magnetic resonance (MR) imaging and computed tomography (CT) are good at providing anatomical information. Three-dimensional functional information about tissues and organs is often obtained with radionuclide imaging modalities: positron emission tomography (PET) and single photon emission tomography (SPET). In nuclear medicine, such techniques must contend with poor spatial resolution, poor counting statistics of functional images and the lack of correspondence between the distribution of the radioactive tracer and anatomical boundaries. Information gained from anatomical and functional images is usually of a complementary nature. Since the patient cannot be relied on to assume exactly the same pose at different times and possibly in different scanners, spatial alignment of images is needed. In this thesis, a general framework for image registration is presented, in which the optimum alignment corresponds to a maximum of a similarity measure. Particular attention is drawn to entropy-based measures, and variance-based measures. These similarity measures include mutual information, normalized mutual information and correlation ratio which are the ones being considered in this study. In multimodality image registration between functional and anatomical images, these measures manifest superior performance compared to feature-based measures. A common characteristic of these measures is the use of the joint-intensity histogram, which is needed to estimate the joint probability and the marginal probability of the images. A novel similarity measure is proposed, the symmetric correlation ratio (SCR), which is a simple extension of the correlation ratio measure. Experiments were performed to study questions pertaining to the optimization of the registration process. For example, do these measures produce similar registration accuracy in the non-brain region as in the brain? Does the performance of SPET-CT registration depend on the choice of the reconstruction method (FBP or OSEM)? The joint-intensity based similarity measures were examined and compared using clinical data with real distortions and digital phantoms with synthetic distortions. In automatic SPET-MR rigid-body registration applied to clinical brain data, a global mean accuracy of 3.9 mm was measured using external fiducial markers. SCR performed better than mutual information when sparse sampling was used to speed up the registration process. Using the Zubal phantom of the thoracic-abdominal region, SPET projections for

Methylenediphosponate (MDP) and Gallium-67 (^{67}Ga) studies were simulated for 360° data, accounting for noise, attenuation and depth-dependent resolution. Projection data were reconstructed using conventional filtered back projection (FBP) and accelerated maximum likelihood reconstruction based on the use of ordered subsets (OSEM). The results of SPET-CT rigid-body registration of the thoracic-abdominal region revealed that registration accuracy was insensitive to image noise, irrespective of which reconstruction method was used. The registration accuracy, to some extent, depended on which algorithm (OSEM or FBP) was used for SPET reconstruction. It was found that, for roughly noise-equivalent images, OSEM-reconstructed SPET produced better registration than FBP-reconstructed SPET when attenuation compensation (AC) was included but this was less obvious for SPET without AC. The results suggest that OSEM is the preferable SPET reconstruction algorithm, producing more accurate rigid-body image registration when AC is used to remove artifacts due to non-uniform attenuation in the thoracic region. Registration performance deteriorated with decreasing planar projection count. The presence of the body boundary in the SPET image and matching fields of view were shown not to affect the registration performance substantially but pre-processing steps such as CT intensity windowing did improve registration accuracy. Non-rigid registration based on SCR was also investigated. The proposed algorithm for non-rigid registration is based on overlapping image blocks defined on a 3D grid pattern and a multi-level strategy. The transformation vector field, representing image deformation is found by translating each block so as to maximize the local similarity measure. The resulting sparsely sampled vector field is interpolated using a Gaussian function to ensure a locally smooth transformation. Comparisons were performed to test the effectiveness of SCR, MI and NMI in 3D intra- and inter-modality registration. The accuracy of the technique was evaluated on digital phantoms and on patient data. SCR demonstrated a better non-rigid registration than MI when sparse sampling was used for image block matching. For the high-resolution MR-MR image of brain region, the proposed algorithm was successful, placing 92% of image voxels within ≤2 voxels of the true position. Where one of the images had low resolution (e.g. in CT-SPET, MR-SPET registration), the accuracy and robustness deteriorated profoundly. In the current implementation, a 3D registration process takes about 10 minutes to complete on a stand alone Pentium IV PC with 1.7 GHz CPU and 256 Mbytes random access memory on board.