Markov chain modeling of ECG-gated live left atrial fluoroscopy variability to establish a well-defined basis for rigid registration to a 3d CT image.

by

Shivani Ratnakumar, B.A., M.S.

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ABSTRACT

MARKOV CHAIN MODELING OF ECG-GATED LIVE LEFT ATRIAL FLUOROSCOPY VARIABILITY TO ESTABLISH A WELL-DEFINED BASIS FOR RIGID REGISTRATION TO A 3D CT IMAGE.

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Real-time 2-dimensional X-ray to acquired 3-dimensional computed tomography (CT) image registration is currently of interest for improving visualization in the fluoroscopy guided catheter ablation treatment of atrial fibrillation. An important feature of this registration is 3d pose estimation of the left atrium from the 2d fluoroscopy image prior to registration. Computational complexity constraints on this real-time application limit registration to rigid methods. Aimed at satisfying the rigidity assumption, ECG gating is employed to acquire images at fixed phases of the cardiac cycle to circumvent the otherwise continuous elastic deformations of the cardiac chamber. Observations of the ECG gated fluoroscopy sequences, however, yield dynamic variability in the location of registration landmark features across the image sequences. There is currently no protocol for identifying which gated fluoroscopy frame to use in the rigid registration to the CT image. As such, the registration process is not sufficiently well-defined to address the issue of 3d pose estimation. A standard protocol for establishing a well-defined registration representative from the fluoroscopy images is therefore desired. This thesis presents a novel Markov chain method as such a protocol. In this method, patient specific Markov chains are identified from patient data. Empirical transition matrices and the associated unique limit distributions are defined and used to identify a set of registration points. The method was tested on sequences of patient ECG gated left atrial fluoroscopes. A notion of optimality in a set of representative registration points is defined and optimality measures designed to quantify these components were computed and compared to points identified by two

control methods. The results indicated that the MC identified representative points converged rapidly to a stable set once a threshold level of input sequence length was reached. Comparison with the control methods indicated that the MC method was an improvement in each of the optimality measures over the existing random approach. Additionally, the MC method showed optimal stability over the other methods with respect to longer data sequences. This has positive implications for the ablation procedure that follows registration. The well-defined registration representatives form a rigid basis for addressing the challenge of 3d pose estimation from the fluoroscopy images. This is discussed in the context of ongoing and future work.

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Shivani Ratnakumar

Contents

List of Abbreviations

1. 2d = 2 dimensional
2. 3d = 3 dimensional
3. AF = Atrial Fibrillation
4. CS = Coronary Sinus
5. CT = Computed Tomography
6. ECG = Electrocardiogram
7. FLE = Fiducial Localization Error
8. FRE = Fiducial Registration Error
9. LA = Left Atrium
10. MC = Markov Chain
11. PV = Pulmonary Vein
12. PVR = Pulmonary Venous Region
13. RSS = Residual Sum of Squares
14. SVD = Singular Value Decomposition
15. TRE = Target Registration Error

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Chapter 1

Introduction

1.1 Overview of Problem

Medical image registration is the alignment and superimposition of at least two differentially acquired medical images of a single anatomical region. One image is chosen as a reference, while the other is geometrically manipulated to match its size and orientation. Registration is achieved when the manipulated image is superimposed onto the reference. This creates a single fused image which contains all the visual information provided by the individual component images. The registered images can either be from a single imaging modality or from different ones depending on the goal of registration and the available images.

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the United States. During AF, the atria of the heart experience episodes of rapid, but weak heartbeats. One of the causes of AF is believed to be errant electrical impulses originating in the left atrium (LA) and pulmonary vein (PV) regions. Of interest in this thesis is the treatment of AF by ablating the region around the PVs to electrically isolate them from the LA. Ablation is performed by applying a radio frequency current to the targeted sites through an ablation catheter placed in the LA. The ablation catheter is navigated to the target sites by a cardiologist whose main visual guide is a live X-ray feed showing the location of the catheter but no other structural detail. The success of the treatment depends largely on accurate ablation. Inaccurate ablation could result in a recurrence of the arrhythmia. Stenosis of the pulmonary veins is another potential consequence of inaccuracy, with high costs to patient health.

There are increasing trends in morbidity and co-morbidity of AF which are associated with increasing costs to patient health and to health care. Consequently, there is growing interest in developing improved treatment techniques. This thesis centers on an effort to use the registration of live X-ray images to an acquired 3d CT of the left atrium to improve visualization for catheter navigation. The single view containing both 3d structural detail and real-time ablation catheter location information improves visualization for the cardiologist. This has the potential to improve accuracy and speed in the ablation procedure. These benefits, however, are dependent on accurate alignment of the X-ray and 3d CT-derived images. Unfortunately, in the context of this application, accuracy has been difficult to establish. The complexity of the structure and movement exhibited by the cardiac chamber distinguish this registration problem from other medical image registration problems. Additionally, the real-time constraints of the application require an assumption of rigidity on a non-rigid anatomical region, with unique implications.

Registration accuracy is dependent on the alignment of regions of interest, or target regions, in the component images. It is generally the case in medical image registration that the target region is not discernible in all the images involved. As such it is not uncommon that indirect measures be used to form an estimate of registration accuracy. In some cases this is a well studied and understood problem. However, those cases involve more rigid anatomical regions where the alignment of target regions can be correlated to the alignment of other discernible features. In the registration of CT and X-ray cardiac images, the difficulty in evaluating registration results stems from the lack of discernible features in the X-ray image. Further, the amount and complexity of elastic movement experienced by the heart makes it difficult to apply the known methods of error estimation. Electrocardiogram (ECG) gating is employed with the aim of satisfying the rigidity assumption on the application. However, as will be discussed, visible variability in ECG-gated fluoroscopes of the LA indicate that ECG-gating is insufficient to completely circumvent cardiac motion. Addressing this insufficiency is the central part of this thesis. Additionally, this registration is 3d to 2d. Interdimensional registrations require an estimate of the 3d orientation of the imaged region in the 2d projection image. This is known as 3d pose estimation and must be conducted prior to registration. This difficulty in performing a pose estimation from a 2d cardiac fluoroscopy image is compounded by the variability witnessed in the ECG-gated images.

The uniqueness of this CT to live fluoroscopy registration and the considerations required due to the complexity of cardiac structure and dynamics necessitate a novel approach to ascertaining registration accuracy. The following section presents the current status of 3d to 2d and cardiac image registration, leading up to a statement of the thesis in Section 1.3

1.2 Present Status of Problem

Cardiac image registration has received increasing amounts of attention over the last decade. Cardiac imaging systems are now common place and registration is often invoked to optimize the information contained in the images. Left atrium (LA) image registration, as a navigational tool in the surgical treatment of atrial fibrillation (AF), is the specific area of interest in this thesis. It is believed to have the potential to improve accuracy and reduce procedural time in this minimally invasive (in the context of surgical treatment of AF) treatment. Numerous recent studies identify an increasing incidence of AF, and its associated health and monetary costs.[105][135][37] This has led to active interest in improving treatment tools and techniques and there are currently numerous groups working on various types of LA image registration applications.[25][26][58][60][91][114][119] Given the sensitive nature of the ablation process, accuracy in ablating is essential, placing demands on the accuracy of the registration applications. Thus far, however, error analysis of LA image registration has not received much attention. This thesis will address issues surrounding error analysis in 2d to 3d LA image registration. The discussion of the problem's present status herein, thus, spans a few areas of medical image registration and the advances that have shaped the current problem.

Image registration has been successfully employed in such fields as neurosurgery and oncology as an aid in diagnostics and treatment planning and execution. The technique is fairly common in these and other medical fields, and is currently used with confidence. The fields that have seen the most success with the clinical use of image registration are all ones in which rigorous validation studies have been carried out. These fields involve anatomical regions whose geometry and function are comparatively easiest to characterize. This is because these situations allow the generation of realistic simulated data (whether based on computer simulation, phantom data or image database information) with which rigorous in vitro tests can be conducted. It is the in vitro tests that generally form the gold standards against which registration methods are measured before being clinically tested. Gold standards provide a benchmark for evaluating novel registration techniques. In the case of cardiac image registration, however, the complex anatomy and mechanics of the heart are difficult to characterize. In vitro testing of registration methods has been limited to techniques such as using static phantoms, yielding results that have not captured the essence of the problem. In these cases, it is often acknowledged in the discussion that observed accuracy levels may be reduced in a clinical setting due to movements.

The majority of registration applications and subsequent validation studies address 2d to 2d or 3d to 3d problems. These are well-studied in the non-cardiac context, and registration evaluation techniques, such as Holton et al's, 1995, validation paradigm for 3d to 3d image registration[46], are easily found. When images of different dimensionality are registered, one of the image spaces has to be shifted to that of the other, either at a loss or gain of one dimension. This adds an additional source of error to the registration process, and requires special consideration in validation studies. Numerous gains have been made in recent years, to improve inter-dimensional registration problems, and in 2005 a standardized evaluation methodology for 2d to 3d registration[131] was proposed and is currently in use. This method, however, evaluates the registration software, independently of the anatomical region being imaged. As such, it provides a current gold standard by which to evaluate 2d to 3d registration algorithms. Certainly, the standardized evaluation would help in evaluating the technical soundness of a 3d to 2d cardiac image registration method, but would still not address the complexities that arise from the nature of the imaged cardiac chamber itself.

3d to 2d registrations applications arise primarily where there is a need to incorporate structural or functional detail with a real-time image. In these applications, 3d pose estimation is an integral and well-studied component. The 3d pose, or orientation, of the object represented in the 2d image has to be estimated in order for an alignment of the two image spaces. Two standard ways in which pose estimation is approached are bi-plane fluoroscopy and ray casting.[9][26][142] Bi-plane fluoroscopy creates two orthogonal projections of the anatomical region and aims to use the combined projected information to reconstruct the object's 3d position. Ray casting mimics the action of an X-ray projection on a 3d image data set, creating 2d associated datasets for each projection. The 3d volume is incrementally rotated and projected datasets are recomputed and compared to the 2d image. The process is repeated until a pre-determined degree of similarity is achieved between a projected dataset and the 2d image, thus identifying the 3d orientation of the imaged object. Both of these methods are computationally complex, however.

The field of cardiac image registration for intra-procedural navigation is new and fast growing. While the literature clearly acknowledges validation as a vital step in any registration effort, this aspect of the problem has not been the focus of attention. The majority of effort has been placed in developing methods for registering cardiac images, based on ideas developed in other fields of medical image registration. These methods utilize the latest technical advances found in other fields and the latest cardiac image acquisition processes to best suit the rigid registration implementation. However, there is little discussion in the literature about methods of appropriately testing these registration methods. Most of the LA registration validation work that has been done involves clinical trials in which accuracy is difficult to establish. Recurrence rates and the incidence of pulmonary vein (PV) stenosis, a consequence of inaccurate ablation, are the main means by which accuracy is currently discussed in the context of AF ablation treatment. As discussed in a 2005 Circulation editorial[127], one of the current questions is how to better measure accuracy in the use of registration for cardiac interventional purposes since there is no leading theory found in the literature. Figures 5.1 and 5.2 in Chapter 5 show the 2d fluoroscopy image and 3d CT rendering that are to be registered for the purpose of catheter navigation for ablation treatment of AF.

A limiting factor in LA registration for catheter ablation treatment is that registration has to be conducted in real-time, while the patient is in the operating suite. This places restrictions on the amount of computational complexity involved in the registration. What would ideally be a non-rigid, elastic, registration of images, in which allowance is made for the soft-tissue deformations observed in the heart, has to be simplified to a rigid registration.[116] In rigid registration, the imaged objects are assumed to be rigid structures whose orientations can be aligned by a sequence of scaling, translation and rotation. Rigid registration problems have a small, finite, number of parameters to be determined, which allow them to be solved quickly.[40][43] In non-rigid registration, the extra deformations allowed between images add a significant number of parameters to the registration problem. Thus, although non-rigid methods would be ideal for cardiac image registration, the time constraints on intra-procedural registration require the use of rigid methods. Truly rigid body registration problems are well-understood - indeed, in 1998 Fitzpatrick[32] developed a closed form estimate of error in certain types of rigid body registration. Simplifying assumptions of rigidity have been used in registration methods which involve other anatomical regions, since no part of the human body is truly rigid.[08][59][75][94] However, the known methods of error estimates are not expected to apply with complete accuracy in these cases, since the objects are not truly rigid. Validation in these situations has also proven to be challenging, with a number of studies relying on animal experiments and external skin markers.[68][75][90][91][114][117] The degree of non-rigidity of the cardiac chamber, and its almost (but not exactly) periodic beating mean that careful measures have to be taken in order to make the assumption of rigidity. ECG- and respiration-gated image acquisition are the main measures currently looked upon to