Interdisciplinary Approach to Multimodal Image Fusion for Vulnerable Plaque Detection

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Abstract— **In diagnosis, planning, intervention and monitoring of the potentially fatal Coronary Artery Disease multimodal medical imaging plays an important role. Medical cardiac images of patients suffering from Atherosclerosis exhibit information on cardiovascular plaque that can cause a sudden death due to its vulnerability. The identification of vulnerable plaque is an important research field and can be supported by the use of multimodal image fusion combining anatomical as well as functional information in one image medium. Image fusion has proven to enhance critical components of the multimodal data sources that enable improved diagnostics and intervention. The advancement of image fusion techniques and an intelligent selection of multimodal medical image combinations in the context of vulnerable plaque detection require an interdisciplinary approach. This paper reports on the first achievements of a collaborative research project involving clinicians and image processing engineers. During the first stage an interdisciplinary workflow was established. Critical research questions were identified. The second phase will concentrate on image processing to fuse selected multimodalities to obtain images of higher quality which will ease the daily work of the clinicians and reduce invasiveness for the patients.**

Keywords: Interdisciplinary research, coronary artery disease, atherosclerosis, multimodality, vulnerable plaque, medical image fusion

I. INTRODUCTION

Coronary Artery Disease (CAD) is the leading cause of death worldwide. It is expected to increase dramatically over the next 20 years with respect to the ageing of the world population [1]. With the intention to support the development of a solution to this problem a research centre has been established by the National Heart Institute, Kuala Lumpur (IJN) and the Universiti Teknologi Malaysia (UTM). The IJN-UTM Cardiovascular Engineering Centre (Cardio Centre) has been initiated by Dato' Seri Ir. Dr. Zaini Ujang, former UTM Vice Chancellor. A Memorandum of Understanding (MoU) has been signed between UTM, the Rheinisch-Westfälische Technische Hochschule (RWTH) Aachen, Germany and the UTM Board of Directors. The consortium approved the proposal to establish the Cardio Centre on 3rd January 2013.

The Centre serves the purpose of developing human capital in the area of cardiovascular engineering. Besides the Cardio Centre aims to develop technology and products for cardiovascular applications, as well as to implement technology, products and management systems in clinical practice in close cooperation with the affiliated medical institution. The Cardio Centre is divided into four major research clusters, which are (1) Cardiac monitoring cluster, (2) Cardiac imaging, (3) Cardiac devices and (4) Cardiac biomaterial cluster. The research clusters were formed to enable the local production of a low cost artificial heart, stents, tissue, drugs as well as hard and software for monitoring, diagnosis and management purposes.

Within the cardiac imaging cluster, a team of experts in the field of medical imaging and image fusion plus a group of clinicians has gathered to join their efforts for the development of new ways to detect the presence of vulnerable plaque in the artery. The purpose of this research is to concentrate on the optimization of multimodal medical images used at IJN in the context of cardiovascular plaque detection and characterization.

This conference paper is divided into several sections, to focus on different areas in conducting the research. The first section describes the coronary artery disease (CAD). After introducing the problem, the next section discusses modalities that are being used by IJN related to cardiovascular diagnosis, monitoring, planning and intervention. The third section explains the purpose and techniques of medical image fusion, together with the expected outcome of fusing medical images acquired by

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the different modalities at IJN. After that, a section on the current status of the collaborative research is added. Finally we provide an outlook to the planned experiments and expected outcome.

II. Coronary Artery Disease

Atherosclerosis is a disease that is causing the narrowing and hardening of the artery. This disease is a multi-factorial complex disease which is related to inheritance, and traditional and non-traditional risk factors [2]. Plaque is formed in the artery triggered by a damage of the endothelium which then causes atherosclerosis. Plaque identification requires knowledge about the morphological characteristics of the plaque which includes a large lipid core, a thin fibrous capsules, intraplaque haemorrhage deposits and less degree of calcification [3]. The development of plaque initiates from the low-density lipoprotein cholesterol (LDL-C) that is involved in atherosclerosis. The biological processes related to the development are inflammation, neovascularization and mechanical forces [3].

When the smooth lining of the artery is damaged the LDL-C, that is so-called bad cholesterol gets into the wall of the artery [3, 4]. Automatically the human body will send cells, called macrophages, to defend the invasion of LDL-C [3]. Foam cells are formed when the macrophages become enlarged cholesterol-enriched cells and are embedded in the vessel wall. Fatty streaks present in the vessel wall show the foam cells accumulation. The body tries to protect the artery by surrounding it with the fibrous capsule as the fatty streaks grow causing the luminal narrowing [3]. At this stage, the growth is called a plaque. Over time calcium may be deposited in the plaque making it hard and inflexible. The increasing blood flow pressure at the narrowing part of the vessel can damage the capsule covering the plaque which may then rupture. The rupture can result in a blood clot that can cause heart attack and stroke [3, 4].

III. Modalities Used in Plaque Detection

Due to the dangerous nature of vulnerable plaque it is important to detect this type of plaque and possibly predict its behaviour. The relatively slow progression of atherosclerosis may unpredictably become fatal [2]. The modalities used at IJN for cardiovascular investigations are Echocardiography, Magnetic Resonance Imaging (MRI), Optical Coherence Tomography (OCT), Intravascular Ultrasound (IVUS), Computed Tomography (CT) and Angiography. The project team established an interdisciplinary communication between engineers and clinicians to identify potential multimodal image interpretation using advanced fusion techniques. As a first result the team extracted current practices and workflows in the context of plaque detection and monitoring looking at the different modalities. At IJN the patients do not always undergo multimodal data acquisition. In most of the cases a diagnosis is anticipated from Echocardiography because it is a low cost, non-invasive method to acquire information. In certain cases an additional CT is required (3D anatomical information). CT provides high resolution but has an invasive component due to the radiation exposure. MRI is used to obtain additional input for diagnosis verification (anatomical and functional information, in particular on the soft tissue). For patients where the disease status is clear from history or Echocardiography often an invasive coronary angiogram allows direct diagnosis conformation and intervention. The understanding of the techniques used and the function of each modality is essential for this project.

A. Echocardiography

Echocardiography uses acoustic signals (ultrasound - US). In visualizing the cardiac condition, echocardiography has shown to be highly versatile and beneficial [5]. Echocardiography uses the concept of ultrasound where a signal with a diverse velocity is transmitted into the body and reflected between tissues of different density [6]. Using echocardiography allows the clinicians to recognize complications of myocardial infarction. Other than that, echocardiography shows the abnormalities that may precede the development of heart failure. Multiplane Transesophageal Echocardiography as applied at IJN allows an understanding of the status of the functionality of the heart even though the spatial resolution is very variable. Using different views various functional parameters of the cardiac performance can be measured. A disadvantage is the dependence on the operator. US is strongly dependent on the skills of the operator involved and requires a lot of manual experience to provide meaningful data. Echocardiography allows the identification of plaque based on the high reflection of calcified areas. Using a 3D probe the transesophageal echocardiogram (TEE) permits different views of the cardiac structures. One of the main advantages is the superior temporal resolution, far greater than CT or MRI. Other advantages of Echocardiography are its non-invasive characteristics, low-cost and mobility.

B. Magnetic Resonance Imaging

As stated by Corti et al. [7] MRI is projecting radiofrequency pulses onto a subject that is placed in a strong magnetic field. The application of MRI is used to show different plaque components on the basis of biophysical and biochemical parameters. MRI produces ionizing radiation and can be repeated sequentially over time because the patient is not exposed to endangering radiation. Another advantage of MRI is the simultaneous acquisition of anatomical and functional data that allows complex analyses and increased diagnostic capability. MRI is mainly used for stress perfusion and viability studies related to soft tissue and blood flow.

C. Computed Tomography

Computed tomography (CT) can detect and quantify the presence of a non-calcified atherosclerosis of a coronary artery [2]. Even though only a minority of atherosclerosis is calcified, it has been stated by experts that there is a direct relationship between the degree of coronary calcium and the degree of coronary atherosclerosis [8]. CT is very strong in analyzing blood vessel anatomy and reconstructs the real shape of the heart from the acquired slices at high spatial resolution. CT is invasive based on the radiation to which the patient is exposed.

D. Intravascular Ultrasound

Another technique that is applied for diagnosing atherosclerosis is intravascular ultrasound (IVUS). The most commonly used modality for diagnosing CAD is the 20-45 MHz range IVUS [4]. IVUS can penetrate through luminal blood and into the vessel wall with the depth of more than 5mm. With the large penetration, IVUS can provide the clinicians the images vessel remodeling, lumen size and plaque morphology. IVUS may give insufficient image of vulnerable plaque [4]. However, IVUS is an important modality to allow precise measurements needed for planning and intervention.

E. Optical Coherence Tomography

Another modality which uses an optical approach is Optical Coherence Tomography (OCT). OCT has a high-spatial resolution in mapping of microvasculature, which is a portion of the circulatory system composed of smallest vessels. This modality uses a technique which is based on low-coherence interferometry principle. The advantages of using OCT are being contactless and having more depth in resolving the location of cross-sectional imaging in biological system [9]. Images that have been generated by OCT are based upon back-reflected light from the sample. OCT allows precise measurements of plaque burden, vessel size, degree of stenosis and others. It facilitates recognition of thrombus, fibrotique plaque, lipid lodge plaque and calcification.

OCT and IVUS have different advantages and disadvantages and result in complementary data. OCT offers high spatial resolution but has less penetration into the vessel walls. IVUS in the contrary provides less resolution but allows acquiring information about vessel walls due to deeper penetration. However the availability of OCT and IVUS data for one patient is rare. The choice of imaging modality always depends on the information that the clinician is looking for. If necessary only one additional modality is selected: either OCT or IVUS.

F. Angiography

The last modality that is taken into consideration for the purpose of this project is coronary angiography. A special dye (contrast material) is injected to perform coronary angiography together with x-rays to visualize the blood flowing through the arteries. The dye makes the coronary arteries visible on x-ray images. This helps the clinician to see blockages in the arteries and blood flow performance in general.

IV. MULTIMODAL MEDICAL IMAGE FUSION

As previously stated different modalities offer different features. For instance, images of MRI capture the different plaque components whilst CT shows the calcification process in the context of atherosclerosis. The described modalities provide information on anatomy and functionality of the heart, in this context in particular of coronary arteries. The heart is a very special organ because it is a moving object which makes the imaging process and data processing rather complex.

A. Definitions

When combining two images from different modalities the result produces a much more reliable image that ideally features both of the original information content [10]. This process is called image fusion. Image fusion is a method to merge multiple input images in order to produce a single output image containing the information of the input images [11]. Multimodal image fusion has the capability to integrate functional and anatomical information as well as to provide different views of the heart which help the localization of the source of the patient's symptoms.

The objective of creating a fused image is to improve the quality of the information contained in the output image. It is a synergetic effect. Image and data fusion find many different applications in the fields of remote sensing, military, biometrics, machine vision and medical imaging.

In medical image fusion it is important to use techniques that avoid artefacts, ensure lossless fusion, and increase usability.

The scientific community has established three levels of fusion rules [12]:

1) Image level (also called pixel or iconic level) is the fusion on a pixel by pixel basis and hence preserving most of the data content [13],
2) Feature level (also called regional or object level) that extracts features from the source images

and combines them into a single concatenated feature vector [13], and

3) Decision level (also called information level) which comprises image sensor information fusion, after the image has been processed for each modality separately. The extracted 'useful' information is fused [13].

B. Medical Image Fusion

The use of image fusion in the medical context is to improve confidence in diagnostics, to provide structural and functional information in the same image, to increase the reading efficiency, to quantify the difference between scans, to plan radiation therapy and much more [14]. From medical image fusion the clinicians can benefit from the complementarities of the different images to decide whether there is evidence showing the progression of the disease. In advancing clinical reliability, medical image fusion (MIF) has proved to be useful for diagnosis and analysis. MIF can be categorized in three parts, which are image modalities, fusion techniques, and organ under study [15].

The image-based fusion techniques used in the medical context concentrate around multiresolution approaches (MRA) such as wavelets [10], curvelets [16] and contourlets [17], Intensity Hue Saturation Transform [18], as well as hybrid approaches, such as IHS/PCA (Principal Component Analysis) [19]. These approaches are being explored in the current experimental research phase of the project.

C. State of the Art

Current research shows effective medical image fuson between two different modalities. An example is the combination of Positron Emission Tomography (PET) with CT or Single Photon Emission Computed Tomography (SPECT) with CT. Both combinations show the advantage of reducing diagnosing time for the patient [20]. Other than that, the advantages of multimodal medical image fusion can reduce the cost of healthcare since problems could be identified at an earlier stage. Fusion can help the clinicians to measure myocardial (muscular tissue of the heart) and vascular structure function interaction [21]. The disadvantages of using this technique is the PET and SPECT use radioactive substances that are injected to the body of the patients. These recent developments have not yet entered operational mode. At IJN no PET or SPECT modalities are available since it is not a general hospital. It would be more cost-effective to have PET-CT if there would be many uses for it, particularly for treating cancer. For cardiac applications alone this type of modality would be too costly to maintain.

D. Practical Consideration applicable to IJN

The aim of this project is to provide least-invasive, efficient multimodal image fusion approaches that reduce impacts on the patient, improve results and ease work pressure on the clinicians. We aim at the development of innovative approaches in multimodal medical image fusion by fusing images of less invasive, yet effective modalities, e.g. MRI/Echocardiography. IVUS-OCT, the large penetration depth of IVUS together with a high resolution OCT can produce and image with clear view of the atherosclerosis [4]. In practice, at least for the case of IJN, simultaneous IVUS and OCT data for one patient does currently not exist. Either IVUS or OCT is used. The contrast that is provided by MRI data can be combined with CT which offers image brightness related to the tissue density to produce an image that contains the both features of MRI and CT [22]. In the case of IJN other useful combinations of different modalities need to be taken into consideration in order to the maximize result for diagnosing atherosclerosis and plaque burden followed by vulnerability assessment. Due to the largely available Echocardiography it makes sense to consider the combination of US data with the other modalities mentioned above.

V. Current Status IJN-UTM Research

In the first period of this project the identification of a significant research focus as well as the establishment of an interdisciplinary communication between IJN clinicians and UTM Engineers had first priority. In the meantime based on many discussions and visits, as well as live observations of multimodality imaging practices at IJN by UTM Engineers it has been agreed to focus on cardiovascular plaque. Ultimate goal of the joint research is to develop advanced medical image fusion processes to enable the identification of vulnerable plaque. Currently the researchers are concentrating on plaque occurrence in the coronary arteries.

The second step in the process of establishing an operational research framework was the understanding of the current workflow in terms of multimodal image acquisition at IJN. Several on-site observations and interviews with the various cardiologists in the different imaging departments resulted in the recognition that different diseases and situation require different observations in terms of modality. In addition there is the constraint that multimodal data acquisitions are costly, time-consuming, and additional stress on the patient.

As a result there are different priorities given to the data acquisition procedure. Most commonly Echocardiography is performed. 90% of the patients being referred to IJN are firstly undergoing Echocardiography. It is fast, non-invasive and relatively inexpensive. Only if the result of this investigation indicates the need for another modality the patient is undergoing further modality data acquisition. In the case that an intervention is required but also for pure diagnosis Coronary Angiography is applied in almost 50% of the cases. It has the advantage that it allows direct intervention during the diagnosing process. Only 5% of the patients admitted to IJN have experienced multiple modalities image acquisitions.

A. Choice of Modalities

The following factors that play a role in the decision process for a certain modality have been identified:

First and most important are the symptoms of the patient. Secondly the patient's history is analyzed. Thirdly, the degree of invasiveness is evaluated to verify the choice. Other factors that are important to be considered in an operational environment such as IJN are costs, availability of a certain modality, consent of the patient and his family, consequences and last but not least the particular clinician's expertise and experience.

B. Research in an operational Environment

Looking at scientific achievements researchers would follow the research path: "What is possible"? In the case of an application oriented research it is necessary to identify "What does make sense"? So the three criteria which constrain multimodal image fusion:

1. Multimodal availability of data for one patient;
2. Invasiveness of different modalities even if the use of multiple modalities would improve the results;
3. Amount of additional value if using multimodal image fusion.

VI. Further Planning and Fusion Experiments

Considering that IJN uses state of the art modalities from different vendors the design of the fusion experiments has to be independent of the modality provider. Looking at the results of the discussions between clinicians and engineers the following combinations of images appear to be useful for obtaining improved interpretation capabilities for plaque detection in multimodal data:

Due to the large availability of Angiograms this modality could be combined with OCT, IVUS, and CT.

Other suitable combinations of modalities are MRI / CT, and various modalities with US.

For the detection of vulnerable plaque the image enhancement will focus on lesions, thrombus, plaque characteristics, its status of cap thinning and calcification. The process will consider their appearance in the various modalities and also comprise secondary information that lead to the conclusion of existence of vulnerable plaque.

The project is now in the process of identifying suitable images to enter the experimental phase. From the practical experiments UTM will establish a feedback loop with IJN to iterate the fusion process until it reaches a suitable stage for practical use in an operational environment.

VII. Conclusions

This research initiative is using a unique collaboration of technical engineers and clinicians. It aims at providing solutions to improve current multimodal imaging practices in the context of cardiovascular plaque detection, focusing on vulnerable plaque. Based on close communication and interaction between the interdisciplinary research team partners it was possible to define the operational workflow. The project is still in an initial phase. The relationship between engineers and clinicians has been established. Data acquisition has been completed. 23 medical data sets containing multimodal cardiovascular plaque observations were collected from all six identified modalities. Currently the data is screened for suitable modality combinations. The project enters the experimental phase now.

In conclusion it can be stated that the practical work of interdisciplinary teams leads to extremely useful results. It ensures the applicability of research findings that create an impact and provide benefits to all parties involved. Without an understanding of the collaborator's expertise no useful outcome can be expected. A common language has to be defined. In addition the research focus should consider daily practice keeping future possibilities and innovation in mind. The expected outcome of this project is a good understanding of current constraints and potential improvement areas. In the field of multimodal image fusion for vulnerable plaque detection the upcoming experimental phase will provide a new workflow and potentially more effective algorithms supporting diagnosis, planning, intervention, and monitoring.

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