Sensors, Actuators, and Devices in Cardiovascular Systems

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Abstract— **This paper presents a literature as well as technology review of the most recent conducted research efforts and technology achievements in the cardiovascular treatment field. This review is aimed at providing future researchers and developers with major highlights on efforts and achievements in direct relation to sensors, actuators, and devices as applied to cardiovascular system monitoring, mapping and imaging, diagnosis, and treatment. The review concludes by indicating areas of high importance and future potential for further investigation and by listing future investigation topics as considered of special interest to the author.**

Keywords— **cardiovascular, imaging, actuators, sensor,**

I. Introduction

The evolving life style has contributed over the last few decades to elevating heart diseases at unprecedented rates. In the US alone, it is estimated that over half a million die each year because of heart-related conditions [1]. Additionally, over one billion people worldwide suffer from hypertension [43]. However, it is anticipated that significant life savings along with significant health care cost savings can be achieved with certain precautionary measures, involving mainly monitoring, diagnosis, and preventions ones. The accelerated developments and technology advancements in the field of sensors and associated devices for cardiovascular related applications provide promising achievements to reduce the evolving heart diseases and risks [3]. Technology advancements range from patient-site applications to on-line monitoring ones.

A careful look at the developed applications needed in the different areas and stages of the cardiovascular system treatment indicates clearly that these applications "except for drugs and medications" consist of either sensors or actuators or a combination of both. These applications are usually "and mostly for regulatory classification purposes" called medical devices. Whether the medical device is a catheter actuated mechanically to perform a mechanical objective, or it is a battery-powered pacemaker to regulate heart beats, or it is an external or embedded pressure sensor, they are all described as medical devices of different classifications.
Therefore, that indicates "once again" the great involvement of sensors and actuators in the different stages of heart-related treatment ranging from the monitoring and precautionary measures of a healthy one through to the diagnostic applications and all the way to the treatment and post-treatment stages. Investigation of the most recent research efforts and technology achievements indicates that efforts are focused on certain main areas including 1- imaging and mapping, 2- monitoring, 3- diagnosis, and 4- treatment. Efforts in each area include many sub-categories ranging from fundamental analysis, modeling and simulation all the way to sophisticated end user applications. Efforts might also present multiple approaches to the same problem or issue, a point of special importance to researchers, as it highlights new approaches and methodologies and elevates awareness to associated issues and possible problematic areas.

The cardiovascular system and the heart diseases and associated problematic issues is a highly complex and yet very sensitive area naturally for the very obvious reasons, and the research and development in this area are therefore of the same complexity level but yet very crucial to explore. It is for these reasons among many others that a thorough literature review is conducted to establish a solid background for more mature understanding of the most appealing cardiovascular system related issues, to develop a more elevated understanding for new novel approaches and improvements, to investigate the most recent research outcomes and state-of the-art technology achievements, and to explore the different possibilities for new collaborative efforts and partnerships.

The review presented in this work explores both fundamental research efforts as well as technology advancements and trends. Despite the fact that this is not an exhaustive review "as that might require much more time and space beyond the scope of this work", it presents the most recent efforts and, more importantly, the most appealing and demanding issues from technology point of view. Within the scope of this review, areas that are deemed to be of high importance and future potential are highlighted as "hot topics" as it might be of specific importance and interest for future research considerations. Finally, a brief description of the author's current work area is presented in relation to the review topic, as well as brief highlight of intended future work topics and research interests.

II. Imaging and Mapping

The topic of imaging and mapping is of special interest in cardiovascular treatment because of its direct involvement in all treatment stages. Whether we are dealing with a "presumed" healthy heart, or diagnosing a patient for certain symptoms, or operating on a patient's heart, or post monitoring and post treating a heart patient, imaging procedures are always present. Considering the variety of patient conditions, ages, and treatment type and stage, different imaging techniques are always required to adapt for these varying factors. For this reason "among others", it is noticeable that research efforts and development advancements take the biggest space amongst other areas in the field.

Intensive efforts have been allocated by different research groups to investigate existing imaging techniques and to innovate new ones as well as to improve and/or modify existing ones. Among the most pronounced imaging techniques is cardiac magnetic resonance (CMR), which is considered an important and versatile clinical tool for evaluating known and suspected heart diseases due to the ability to change its characteristics by modulating pulse sequence and parameters. More importantly, this technique is considered one of the most powerful non-invasive diagnostic tools for myocardial anatomy, function, perfusion, viability assessment, and other coronary artery diseases [6, 12].

A major challenge facing the use of CMR is attributed to the continuous motion "and the consequent position change" in harmony with its heart beat rate and mode, which implies difficulties of synchronizing imaging time. However, the development of different CMR techniques has minimized the effect of this challenge by timing image acquisition to the cardiac cycle by ECG gating. Different ECG gating modes were reviewed [6] including single-shot techniques, segmented techniques, and cine techniques. Consequent to these gating techniques, different protocols were developed and used to quantify the case-dependent intensity of CMR. "Anatomic Imaging" protocol is used to provide initial localization of cardiac structure, while "Functional Imaging" is used to obtain images of the heart contractions through the cardiac cycle in multiple orientations using multiple cine-pulse sequences. Miguel et.al. [25] have investigated the performance of semi-automated segmentation method for the anatomical and functional assessment of both left and right ventricles from cardiac cine CMR, and a new quantification technique was proposed which allows for a faster and more accurate assessment of both ventricles Additionally, tissue characterization can be obtained by additional pulse sequences through what is called "intrinsic magnetic relaxation times". Other modes of CMR applications (Fig. 1) include myocardial perfusion, myocardial scarring and fibrosis. CMR is also used intensively in the diagnostic evaluation of coronary artery diseases (CAD), myocardial edema, microvascular obstructions, ventricular thrombus, heart failure, cardiomyopathies, and infraction and viability assessments [6], [12]. Considering that CMR uses a strong magnetic field (30,000-60,000 times the earth's magnetic field strength) to detect the location and properties of protons in the body, special attention is always paid in research to more efficient gating techniques on both software and hardware levels. Different researchers have elaborated on evaluating the different gating protocols and on developing new techniques.

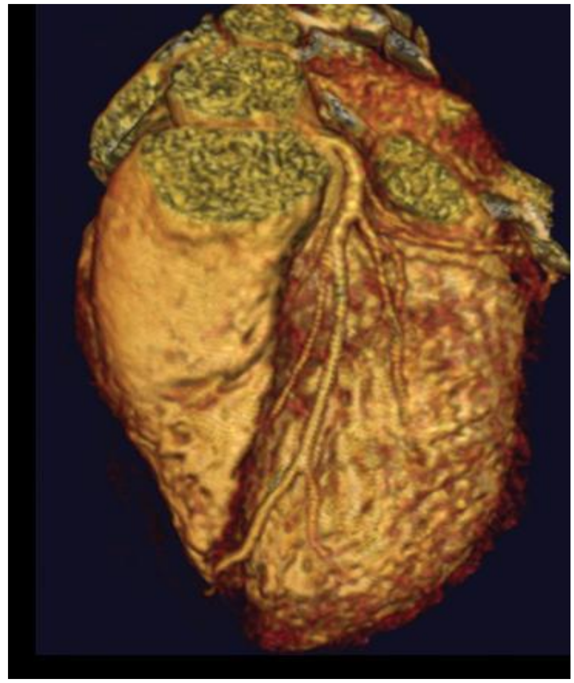

Fig.1 Whole heart coronary MRI angiography

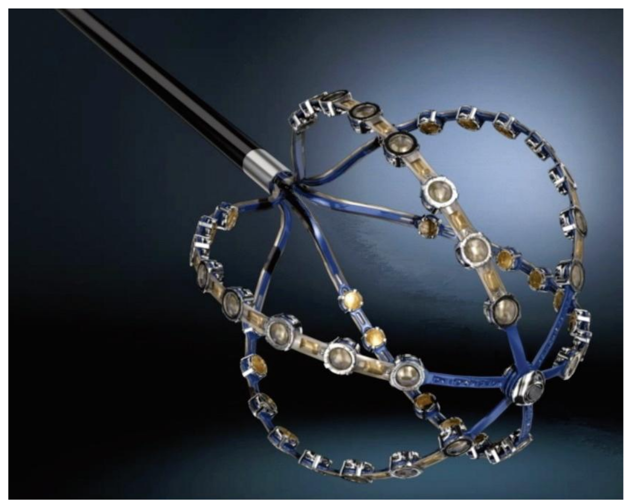

Fig. 2 The "Katheter" by "Acutus Medical" is part of a system designed to construct 3-D images and maps of the heart electrical activation using ultrasound micro-transmitters and sensors.

On both software and hardware levels [25], [38], [41] in efforts to reduce patient interface to CMR, especially fetus, pregnant, premature, and advanced stage patients. Thiel and Seifert [38] have proposed a novel approach in which an ultra-wide band sensor is used remotely (UWB radar) especially for ultra-high magnetic resonance environments. The approach has shown that the UWB along with appropriate signal processing can enhance imaging resolution in CMRI. Martyn et al. [41] have developed an MRI-compatible system to enable scanner gating to the heartbeat of fetus (fECG) for different imaging applications with no adverse effects. Their study has proven the possibility of safely gating CMRI scanner using a modified fECG and a carbon fiber lead system.

On the technology front, many advancements were recently revealed. Among the many examples, GE Healthcare has recently introduced a new CMR technology for its "Signa MRI Scanner" along with a state-of-the art software called "Viosworks", both to simplify MRI scanning through automating imaging sequence to achieve full 3D imaging.

Another interesting avenue in cardiovascular imaging is the 3D mapping of the system. Major firms such as "Topera" and "Acutus Medical" are leading the way in this field through their recently presented 3-D imaging and mapping products (Fig.2). However, it has been stressed that this specific area of the technology is still at early stages and therefore there is still a plenty of room for potential innovation, especially for those researchers interested in exploring ultrasound-based actuators and sensors.

One of the most interesting, most active and yet potentially promising research area in imaging applications is the use of fractional flow reserve (FFR) as a technique used in coronary catherization to measure pressure difference across a coronary artery stenosis to determine the likelihood that stenosis impedes Oxygen delivery to the heart muscle (Myocardial ischemia). FFR can be used in developing non-necessarily invasive analysis of heart conditions. Continuous research efforts are allocated [49-54] to investigate the application of FFR in cardiovascular-related analysis of different issues including CAD, acute mayocardial infraction, intracoronary lesions, and ischemia (Fig.4). The investigation by Wasilewski et al [50] has concluded that a clinically verified FFR practice could become a unique non-invasive method for determining which lesions require revascularization, and therefore reducing the number of patients unnecessarily referred for coronary angiography. Gaur et al [53] have investigated and proposed a method for using FFR by coronary computed tomography angiography in identifying ischemia-causing lesions by adding a coronary atherosclerosis plaque to improve the discrimination between stenosis and ischemia (Fig.5). Another study by Li et al [54] has provided, through study group and statistical analysis, rationale evidence supporting the use of guided FFR for long-term routine CAD practices. Similarly, Deepak et al [51] have compared of FFR results with that of stress testing methods in assessing the presence, location and extent of ischemia. The study has concluded in good correlation between FFR and stress methods, which gives rise to the potential use of FFR method as a non-invasive favorite. Additionally, the review by Qi et al [54] has again stressed on the cost effectiveness and viability of FFR as a potential method of choice in determining the functional significance of coronary artery lesions and as a decision making tool for revascularization considerations. On the other hand, Morris et al [52] have investigated the challenges facing the application of FFR methods on a global scale in CAD assessment, and concluded that more research efforts and hard work ship are required before overcoming the many challenges facing the wide application of this highly potential method. Additionally, recent technology advancements have recorded the possibility of using information from regular CT scans to simulate blood flow through 3-D computer models to approximate FFR measurements without the need for catherization. As a technology "non-limiting" example, "HeartFlow Inc." has introduced a technology to simulate heart flow while pin pointing artery-related FFR issues (Fig. 3).

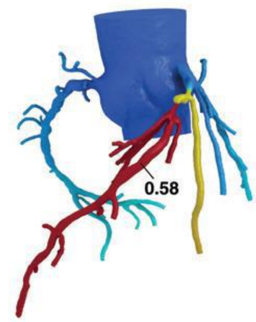

Fig.3 A sample simulated heart model from "HeartFlow" pinpointing red artery as having problematic FFR CT of 0.58.

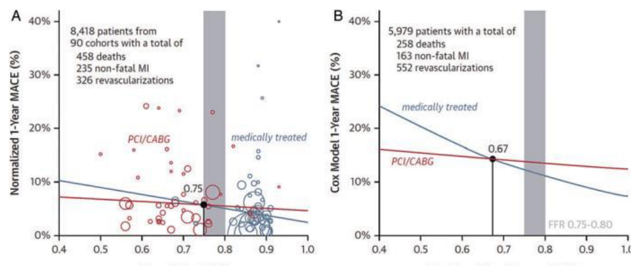

Fig. 4: Progressive importance of FFR values below and above the ischaemic zone [49]

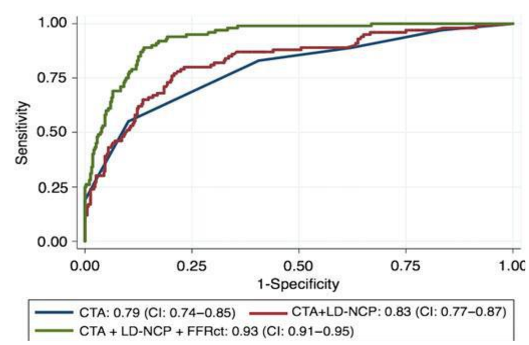

Fig.5: AUCs for discrimination of fractional flow reserve ≤0.80. AUC, area under the receiver-operating characteristics curve; CI, confidence interval; CTA, stenosis severity by coronary CTA; FFRCT, fractional flow reserve derived from coronary computed tomography angiography; LD-NCP, low-density noncalcified PLAQUE.[53].

III. Sensors in Cardiovascular Monitoring

The research in cardiovascular-related monitoring focuses mostly on monitoring 2 parameters as determining factors of heart conditions at any stage, namely pressure and temperature. Literature reviews have investigated [2], [23] the importance of pressure monitoring as well as the different pressure sensing technologies. Piezoresistive and fiber optic sensors [2], [13-15], [20], [23], [48] are among the dominant technologies used. The small foot print, light weight, ability to integrate within catheters and guide wires, low energy requirements, relative low cost and long term capabilities are among the many advantages of fiber optic and piezoresistive sensors. Particularly, the small dimensions, light weight and flexibility of optical fiber-based pressure sensors make them noninvasive, and consequently suitable for in vivo instrumentation in many implantable medical applications. Smith and Abraham [19] have stressed the persistent needs for implantable devices for patients with heart failure (HR) potentials despite their invasive nature, attributed to the capability of such implantable devices in providing real time hemodynamic data remotely. Such devices include mainly right ventricular (RV), pulmonary artery (PA) and left atrial pressure (LAP) sensors, as well as new therapeutic technologies such as cardiac contractility modulation (CCM), and baroreflex activation therapy (BAT). Amacher et al [21] have presented a new numerical control method to optimize the functional interaction between the turbo dynamic ventricular assist devices (tVAD) and the blood circulatory system. A mathematical model was developed and used for the optimization, and the results were validated using a real blood pump in a hybrid blood mock system. Lee et al [22] and Yen et al [40] have investigated the use of Polyaniline conductometric biosensors in the detection of cardiac biomarkers as a method for diagnosing cardiovascular diseases. Linear sensing profiles as well as fast test responses and ultra high sensitivity were presented, an effort that demonstrate potential success of combining bio material and signal processing in an integrated setting (Fig. 6). Detection of cardiac biomarkers were also investigated by [45] using DNAbased biosensors. Poeggel et al [23] have investigated an extrinsic Fabry-Perot interferometer (EFPI) with integrated fiber Bragg grating as a simultaneous pressure and temperature sensor for volume-restricted biomedical applications. The effort exhibits the utilization of highly sensitive fiber-optic based pressure and temperature sensor along with a sophisticated software algorithm, with an all-glass 200µm diameter fiber and a flexible diaphragm tip, making it an evolution for ease of handling sensor even for volume restricted areas. Additionally, other efforts were focused on investigating the capabilities of sensors to monitor more than the pressure and temperature parameters as through impedance plethysmography (IPG), such as the investigation by Theodore et al [43], in which measurements were applied extravascularly directly on large arteries. As demonstrated theoretically as well as by in vivo/ ex vivo measurements, an implantable sensor design was proposed for monitoring cardiac events (Fig. 7).

Supported by FEM simulation and validated by in vivo/ ex vivo real time measurements , the proposed sensor has shown high correlation with blood pressure measurements, which suggests that impedance measurements can be used as a reliable measurement method with good resolutions and excellent signal-to-noise ratios. Based on the non-invasive

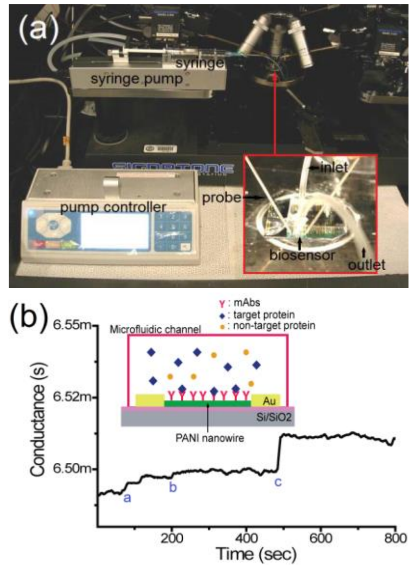

Fig.6: Detection of Proteins using Nanowire Biosensors. Protein levels are indicatives in diagnosing certain cardiovascular system diseases [22].

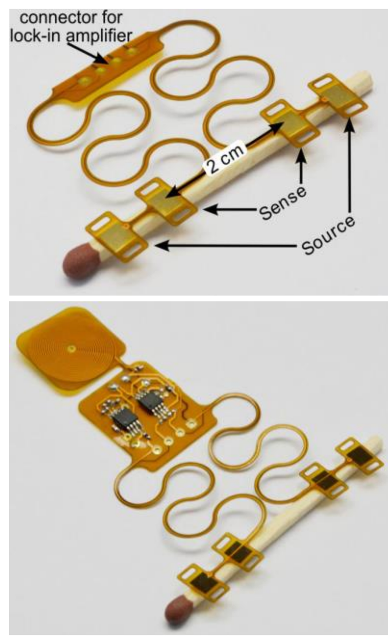

Fig.7: IPG implantable battery-powered sensor using flexible polyimide foil with 4 electrodes placed around the artery to be monitored [43].

advantage of using ultrasound techniques for characterizing the mechanical properties of arteries and consequently in diagnosing different pathologies, Guzman et al [42] have proposed a new analytical semi-rigid method based on "Soft Bodies dynamics" for quantifying elasticity of the different arteries. Different models were evaluated such as "Block Matching", "Kalman Filter", and different optical flow models in order to determine the best model to be used, and a synthetic ultrasound was finally used as the optimum model for simulation. While these efforts investigated implantable sensors, others have also proposed design of externally used acoustic sensors [47] based on the heart sound. Additionally, tremendous efforts are allocated for biosensors, DNA-based biosensors and bio agents [22], [33], [45] in monitoring pressure through arteries and even in disease detection through the monitoring of protein and other fluidic body agents.

Technology advancements were in parallel with fundamental research in focusing on smaller implantable and wirelessly powered monitoring devices. Among the many examples are the "ZIO XT Patch" from "iRythm Technologies" which provides continuous cardiac monitoring for arrhythmias for 2 weeks, Medtronic's "SEEQ Mobile Telemetry System" which provides longer term monitoring, and St-Jude Medical's "Cardio MEMS HF System" which uses an implantable wireless sensor to monitor pulmonary artery pressure (Fig.8).

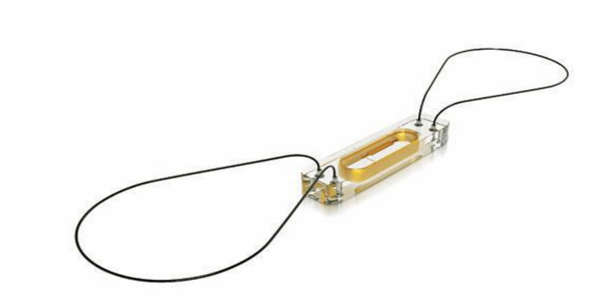

Fig.8 The "Cardio MEMS HF System" uses an implantable wireless sensor to monitor pulmonary artery pressure.

IV. Actuators and Devices

It is almost certain that actuators used in cardiovascular treatments are the end product of case studies based on actual needs and supported by research findings in analytical forms of the physiology, flows, and materials. Therefore, the amount of research around actuators is relatively limited, and most advancements are technology driven. Yet, some research reviews have investigated the theoretical fundamentals in designing proposed solutions for some crucial actuators and devices such as ventricular assist devices [21], in replicating the function of biological muscles [7], and in coronary stents [31].

More advancements are therefore noticed on the technology front. Among the many recent examples, is the leadless pacemakers such as the ones from St-Jude Medical and "MedTronics", were smaller size, lower power requirements, and higher long term reliabilities are among the most desired features (Fig.9).

Other applications focus on actuators as heart implant such as the "CardiAQ" novel mitral valve replacement from "Edward Technologies (Fig.10), the "TandemHeart" percutaneous ventricular assist device "pVAD" and the "ReliantHeart" (HeartAsist5 LVAD) (Fig.11). Fig.8 the "Cardio MEMS HF System" uses an implantable wireless sensor to monitor pulmonary artery pressure. As mentioned earlier, actuators are devices may not be investigated apart from research and investigations in biocompatible materials as fundamental research, which will be briefly reviewed in the next section.

Fig.9 Leadless Pacemakers.

Fig.10 Edward Technologies CardiAQ mitral valve replacement.

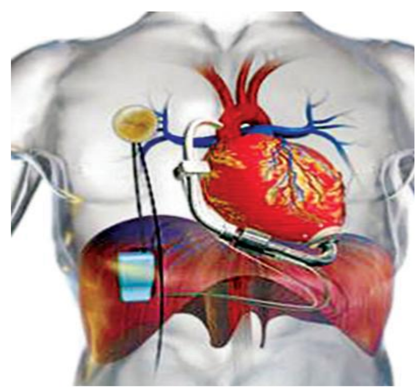

Fig.11 ReliantHeart "HeartAssist5 LVAD" fully implantable LVAD device.

V. Materials in Cardiovascular Systems

Reviews indicate tremendous efforts allocated for researching and developing new materials and technologies to support new advancements and to overcome challenges in cardiovascular applications [8], [9], and [20]. Of course, focus is always on biocompatibility of investigated material with human body [30], [31]. Other researches focus on material characterization and classification for imaging and sensor applications [30], [31], while others focus on the very crucial area of surface modification and particle size control [24], [29], [34-37].

One of the most interesting areas in biomaterial research is the investigation of polymer materials and their applications in cardiovascular sensors, actuators and devices. For example, Morgan [7] has investigated the application of electroactive polymers (EAPs) to replicate cardiovascular devices "mainly actuators" attributed to their ability to replicate biological muscles and their low activation energies in the range of 1-2 volts. Similarly, Sharma [20] has researched the development of miniaturized pressure "sensors on catheter" through the integration of functional nano materials and flexible Microsystems. In this elaborate study, the micro fabrication of the subject sensor from PVDF-based nano material was demonstrated, including all surface treatment stages, all the way to the testing and evaluation of the developed sensor. A variety of polymeric materials are classified for applications in cardiovascular devices and applications, including mainly biostable Polyurethane (BSP's), Polycarbonate Urethanes (PCU's), Biocompatible Drug Delivery Materials, UHMWPE Fibers, and medical grade coatings. All of these categories are characterized by their light weight, toughness, long term durability, flexibility, strength and biocompatibility. Focus on electroactive polymers in cardiovascular applications is apparently one of the most interesting topics and yet an area that requires more investigation, attributed to their potential applications, promising features and characteristics, and low cost.

VI. Wireless Power and Actuating of Cardiovascular Sensors and Devices

This is one of the most interesting topics in the field, as it presents potential challenges for the efficient utilization of developed applications, especially implantable ones. Research in this field focuses mainly on 2 areas: 1- wearable wireless mobile applications for monitoring purposes by presenting solutions to the evolving lifestyle for patients of heart diseases and symptoms. As investigated by Shyamkumar et al [27] and Liu et al [28], advancements in nanotechnology have attributed to the development of textile-based wearable devices in continuous cardiac monitoring. Wireless communication architectures have evolved recently, giving rise to the viability of such devices (Fig.12). Hervas et al [39] have proposed a novel software application and rule-based reasoning engine for patients and physicians. The system suggests using mobile phones for continuous monitoring and therefore communication between potentially diagnosed heart disease patients and clinical/ physician base. A similar solution was proposed by Miao et al [44] which is based on integrating a kinematic sensor built-into the smart phone. Another interesting investigation was conducted by Walsh et al [46] suggesting a wireless-powered implantable atrial defibrillator architecture that facilitates measurements of intracardiac impedance. The investigation has shown promising outcomes, but more importantly it paves the way for future work in this potential field.

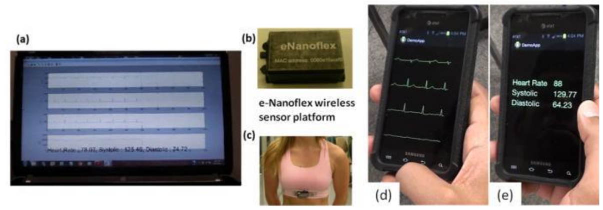

Fig.12: Advancements in wireless communication technologies have evolved, giving rise to the viability of wearable cardiovascular continuous monitoring [27].

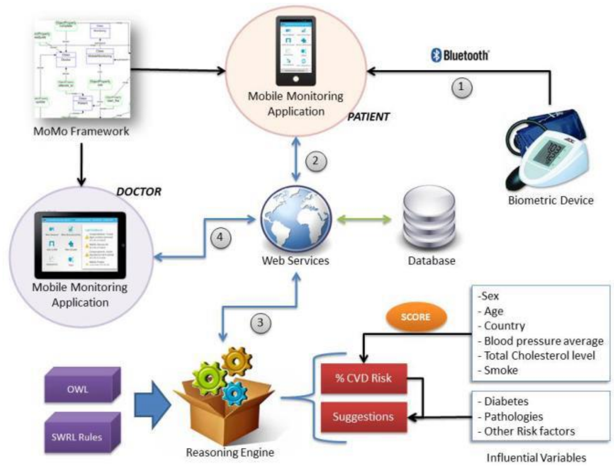

Fig.13: System Overview of software application and rule-based reasoning engine proposed by [39].

2- Which is of more importance is the wireless power transmission to implanted sensors and devices, with focus on transcutaneous power transmission to implantable biomedical devices. As it is of great importance to efficiently transmit powering energy to implanted devices in a human body, different approaches were investigated including adaptive, free-range resonant, and genetic algorithms. Garg and Sredivi [10] have proposed a method for wireless energy transfer to implantable biomedical devices with optimal transfer efficiency (Fig.14). Transcutaneous power transfer methods such as adaptive ones and free range resonant were also investigated [11], [16-17].

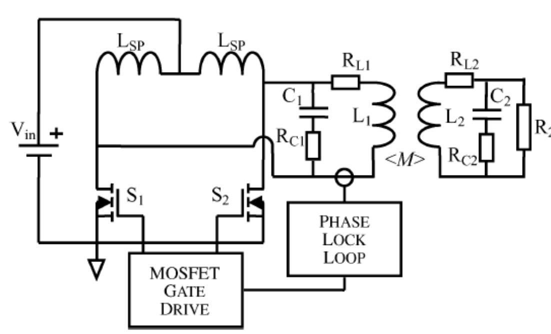

Fig.14: Push-pull parallel resonant converter with parallel resonant pickup [10].

VII. Conclusion

The present review sheds the light "even briefly, and sometimes indirectly" on many crucial information and potential areas of interest to researchers and developers, especially those interested in exploring research opportunities in cardiovascular system related areas. One of the important outcomes of such a review is the Highlighting of what can be called "Hot Research To pics" or "Hot Research Areas". From the author's own point of view, a number of these areas were cited, and can be summarized in the following for those who might be interested:

1-Fractional Flow Reserve Techniques (FFR) as a methodology for non-invasive coronary analysis and estimation.

2- Transcatheter Mitral Valve Replacement (TMVR), which is an area that is still under development and therefore requires collaborative efforts and accumulated expertise in biomedical material and their applications in actuated devices.

3-Transcutaneous power transmission in ventricular assist devices (VAD), as these devices are anticipated to be of great future demands, while efficient and reliable powering is a major limiting factor.

4-Catheter Ablation in Atrial Fibrillation (AFB) treatment.

5-Nano-sized optimally functional devices for minimally-invasive surgeries.

6-Computed Tomography Angiography (Guided Medical Positioning Systems "GMPS").

7- Near Infra-Red Auto Fluorescent Imaging method (NIRAF).

8-Expandable Metal Imaging Modality.

On the other hand, as learned from this review and other related subjects as well as the author's field of research, the author expresses special interest in conducting further future research (based on time and resources availability) in one or more of the following topics of special interest:

1-Simulated heart actuation using ultrasound dipole actuators.

2-Simulated Atrial Fibrillation using embedded ultrasound dipole actuators.

3-Shape memory alloys as actuators for left heart motion simulation.

4-Investigating the use of Electoactive Polymers in simulated heart construction and motion actuation.

5-Investigating the development of biomedical polymers for improved atrial valve durability.

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