SensorART

A remote controlled SENSORized ARTificial heart enabling patients empowerment and new therapy approaches

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Editorial: One year of SensorART

The first year of the Project Coordination has been surely a positive experience. In fact, the Clinical team strongly indicated needs to technical partners while Industrial partners always remembered concrete and realistic plans.

Figure 1 *Snapshot from the 1st review meeting*

The interdisciplinarity of the Consortium obliged to a constructive translation and cultural exchange of different languages. Furthermore, the working hypotheses of the experimental team helped to define a right methodology as well as the protocols for the scientific dossier, by maintaining always the awareness on risk assessment for each step and/or element of the SensorART platform.

For what concern future actions, on one side we plan to implement Synergy pump with pressure sensors (input and output) and flow sensor for a specific platform.

Figure 2 *SensorART overall platform*

On the other side we will define a platform open to other VADs with wearable sensors.

Specific attention will be payed in addressing basic and translational research toward marker detection of heart recovery by temporary unloading and support. As matter of fact, the most ambitious goal of SensorART project is a strategy to recovery.

I would like to underline the continuous, active and friendly participation by All and express my thanks to everybody.

M.Giovanna Trivella
(SensorART project Coordinator)

The SensorART Project has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n. 248763

2007 - 2013

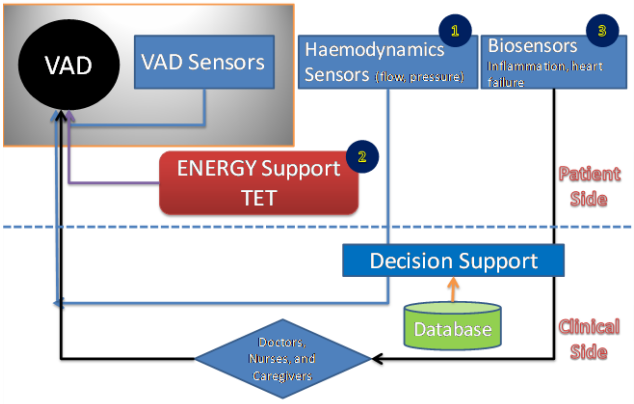
The SensorART project in pills

Project Description

Current treatment of heart failure, in severe end-stage patients, consists of ventricular assist devices (VADs) i.e. mechanical pumps implanted in the patient's body used to restore blood circulation. These devices, whose large majority is constituted by continuous-flow pumps, are nowadays mainly used to provide temporary support (from a few to several months) to bridge heart transplantation. All of these systems suffer from common limitations since they are operated as standalone systems, with no or little regulation capability and substantially unable to interact with the patient and the physicians.

At present, however, VADs are mechanical devices, working in a closed loop, used mainly to bridge heart transplantation.

The SensorART project moves from the idea of realizing an "upgraded device", starting from a mechanical VAD, with the objective of developing an intelligent device, based on an open, interoperable, modular platform.



As shown in the scheme above, the state of art of VADs is represented by the grey area: VADs have motor current sensors and act as "black boxes", in a small, closed loop working in the clinical application. The project has the objective of adding other loops, by including hemodynamic sensors in order to evaluate patient-device interactions and optimize the heart unloading and support. A second objective is substituting the cables, which are the cause of inflammation and sepsis, unfavourably affecting patient's outcome. Replacement of cable connections with telemetric wireless systems for power and signal transmission will increase the patient acceptability. In order to early detect inflammation and to monitor heart failure, the research area of biosensors will be investigated. Finally to obtain a more efficient loop, a decision support system will be implemented, by taking information from physiological sensors, biosensors and existing data base.

The aim of SensorART project can be summed up in three main objectives:

1. to sensorise VADs
2. to allow patients suffering from severe heart failure to conduct normal lives
3. to allow healthcare professionals to monitor patient status remotely and in real-time.

In addition, two more ambitious goals can be identified:

1. to develop VADs not only as bridges to transplant, but also as definitive devices
2. to propose the SensorART platform as a transient therapeutic platform, provided that signals and/or cellular readouts of natural heart recovery will be identified.

In fact, the project will also aim at providing scientists with new knowledge of heart recovery.

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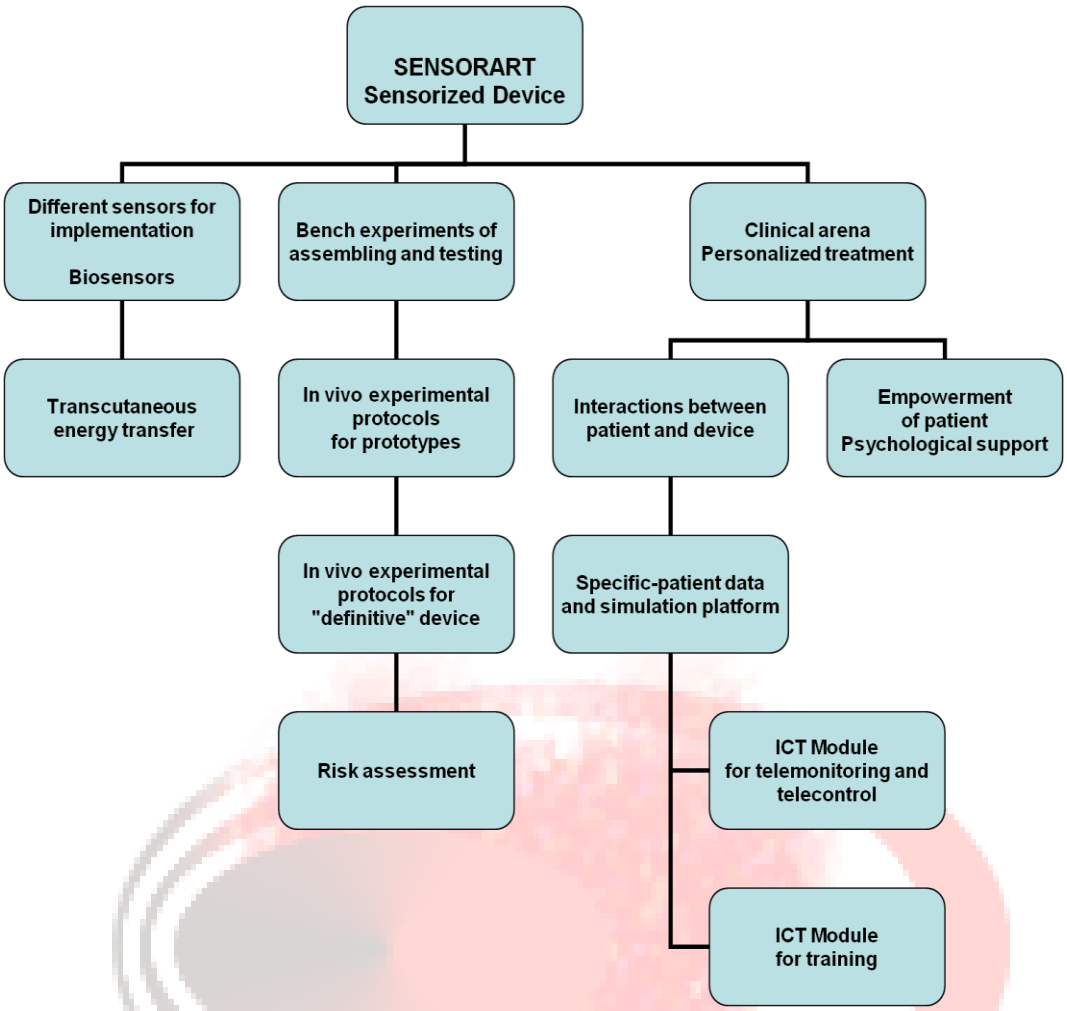
Mechanical artificial hearts are currently used as a bridge to heart transplantation and more recently, as “destination therapy” due to the shortage of heart donors as well as increasing pathology in the aging society.



There is experimental evidence that chronic unloading of the heart leads to improved function of the failing heart. Clinical experiences report the possibility of improving cardiac function to the extent that the patient could be weaned from the device and transplantation avoided. Heart recovery mechanisms and related time are still unknown since today assistance devices are mainly implanted in patients with end-stage heart failure. The clinical significance of such bridge-to-recovery strategy is emerging. It allows the implant of the devices:

- as an alternative to heart transplantation
- in case of life-threatening device-related complications (e.g. recurrent thromboembolism or device infection)
- when urgent transplantation is unfeasible.

Moreover, there is evidence that patients have better quality of life following recovery as compared to heart transplantation and bridge-to-transplantation patients. Heart recovery merits study even in younger patients in whom support allowed good functional recovery, but with low probability of being transplanted and high probability of long-term assistance.

In order to facilitate such a revolutionary approach, the SensorART project aims at better understanding of patient-device interactions by a remote monitoring strategy

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supported by implantable miniaturized sensors (nano- and microsensors) of flows and pressures on VADs (irrespective of their functioning systems, i.e. continuous or pulsatile flow) in order to:

- personalize and optimize the degree of heart unloading
- understand biohumoral signals during assistance, and possible cellular changes before and after the assisting therapy
- measure the capacity of the natural heart to develop major or minor delivery capacity according to the assisting time
- identify recovery times and mechanisms as well as biohumoral signals in assisted patients in order to understand potential outcomes
- steer and optimize pump function without interaction of a caretaker and thus
- improve the patient's independence and quality of life
- reduce the cost in personnel to realize home support.

Physical sensors could also allow assessing the patient/device hemodynamic relationship during assistance, in order to detect the actual and potential contribution of the native heart.

Telemetric wireless sensors integrated in the SensorART platform will allow monitoring of patients after implant.

Patient evaluation can help in adjusting output of the assistance device, by considering the residual cardiac output of the natural heart and the changed needs of the assisted patient (worsening phase and/or acute phase, stabilized clinical state, normal life needs in chronic conditions). From a careful observation of Serious Adverse Events or of the variables changes preceding the events, it would be possible to define new "disease specific" sensors and further implement the devices with specific chemical and/or biological sensors.

The expected results and impact of SensorART project are:

- shift the application of VAD from bridge to transplantation to definitive device also for elderly people
- abolish power supply cables by Transcutaneous Energy Transfer (TET) with improved outcomes and higher patient acceptance
- extend the use of VADs to less severe heart failure extending its possible application to more than 5 million people
- understand the biological mechanisms of natural heart recovery
- extend the application of VAD to short-term treatment of cardiac failure
- empower patients by means of user-friendly ICT devices.

The activities of the project, due to the different areas of disciplines and required competences, are organized in modules, as represented in the flow chart (p.3).

The modules on the left are representing bioengineering laboratories working on sensors, wearable and/or implantable, biosensors, TET, autoregulation unit and telemetric technology. In the experimental laboratories, bioengineering and preclinical research experts work on the implementation of different components, bench testing, experimental protocol definition. The module of risk assessment has the prerequisite of regulatory affairs knowledge and requires a careful evaluation of potential risk in terms not only of implemented device failure, but mainly of its interaction with recipient, i.e. exclusion of lesions of any degree.

Within the clinical arena there are different actions relative to clinical

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requirements definition, data collection from patients, psychological support and personalized empowerment plans.

Data from implanted patient with VAD are analyzed for interactions and utilized for simulation platform, in order to define the ICT modules (telemonitoring, telecontrol, training). Also data from experimental laboratories are collected and processed for ICT modules.

Workpackages Overview

WP1 is responsible for the efficient and productive control of SensorART project. The parts that compose this workpackage are deal with administrative and technical management. Administrative management will promise the internal (inside consortium) and external (with EU) communication, the timely control of progress work, the quality of project deliverables and the efficient financial resource handling. Technical management is responsible for the deliverance of high quality and innovative results inside project's time constraints and specified budget.

The objectives of **WP2** are:

- to define an overall exploitation strategy taking in consideration the partners' specific exploitation models
- to identify internal and external factors affecting SensorART industrial perspectives
- to define business models according to expected SensorART results
- to identify the exploitation environment (macro-environment and market type)
- to analyze the project impact dimension and building the approach on sustainable development, in parallel with the expected results
- to evaluate the existing European legal and regulatory framework, to identify areas able to affect the immediate project's development and applicability in the EU marketplace
- to promote the awareness and, hence, the exploitation of the project's results
- to identify potential stakeholders and to promote activities targeting communication of knowledge and potential project applications .

The objectives of **WP3** are:

- to define and analyze the specific user groups requirements
- to describe the clinical validation plan
- to search the time course of biological markers potentially involved in LVAD unfavourable response
- to involve experts for regulatory requirements
- to collect and analyse policies that represent the legal framework within SensorART will work.

The objectives of **WP4** are:

- development of BioMEMs device that will base on a polymeric substrate and will integrate microsensors arrays and microfluidic structure, which will be made on polydimethylsiloxane (PDMS). The immunosensor will be based on metallic micro/nanoelectrodes. The BioMEMs should allow the multiplexed detection and quantification of proteins by specific antibodies immobilized on gold micro/nanoelectrodes.
- development of immobilisation procedures of antibodies onto functionalised gold micro/nanoelectrodes using Dip-pen nanolithography and optimisation the measurements criteria for impedance spectroscopy in order to achieve immunodetection of proteins in buffer solutions with a detection limit comparable with ELISA tests. The

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experimental conditions for working of an individual immunosensor will also be defined. Finally, electrochemical characterisation of BioMEMs will be performed using blood containing soluble proteins.

WP5 integrates sensors and bio-sensors to meet biocompatibility standards of the VAD, develops a wireless power unit based on inductive coupling compelling with safety norms for variable magnetic fields exposure, releases a prototype for joint integration with the VAD controller and/or sensor nodes and reassures the interoperability and the expandability of the sensorized VAD.

The goal of **WP6** is to develop a VAD independent autoregulation unit. The auto-regulation control algorithm will be implemented in an external and wearable hardware unit, which will be wirelessly linked to the implanted sensors and to the VAD actuators. This unit will allow to autoadjust the blood flow provided by the VAD to the patient's heart according to signals coming from physical and physiological sensors. Moreover, this unit will monitor the energy consumption, as well as the VAD functionality, thus generating the appropriate crucial and vital alert messages. The autoregulation unit will be designed to allow interoperability among different VAD systems.

WP7 provides the Patient's Monitoring Application, the Specialist's Monitoring Application, as well as testing and evaluation of developed applications capability to be used by the clinical workflow.

WP8 provides the VAD – Heart simulation platform and the Specialist's Decision Support System.

WP9 provides the training application based on patient-treatment scenarios, the Research application based on a data collection module and a research database, and a Training Tool for personnel in charge for LVAD.

WP10 deals with the implementation of efficient multi-parametric and adjustable monitoring interfaces, the development of a multi-variant user interface of the specialists' decision support system which will assist the specialist deciding the best remote treatment procedure.

Finally, the goal of **WP11** is to provide acute and chronic animal experiments on sheep and pig models in order to:

- verify the feasibility
- verify the stability of sensors in time in life condition
- assess the biological variability in chronic conditions
- check possible biocompatibility issues (mechanical wear, histopathological findings).

1 Year of SensorART: Preliminary Results

The main achievements of the SensorART project in the first year are summarised in the following.

Dissemination activities have been carried out at various levels, targeting three main audiences: academicians in the field of bioengineering and biomedicine experts, clinicians and general public. In the academic field, the SensorART consortium participated in international conferences and contributed to international scientific journals. Clinicians were addressed by organizing specific events in the framework of SensorART activities. Dissemination at the level of general public has been carried out mainly in the coordinator's country, i.e. Italy, by means of newspapers, television news, scientific magazines, and on the web.

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Dissemination, i.e. presentation of the project outline, scope, but mostly of its results, will probably be more intense and rich in the next years of the project.

In fact, in the 1st year, dissemination consisted in presenting the project (as general outline) and the results of single components (mainly biomarkers and cardiopulmonary circulatory model).

As regards to market potential, a preliminary analysis of the industrial trends in Europe and United States for VAD confirm that the objectives of SensorART can meet the current demand of the VAD market, which consists mainly on a fully implantable system, in order to increase patient comfort and safety, together with a more intelligent system. This last feature could provide an optimization of the VAD therapy as well as an enhancement of the device monitoring capability.

A preliminary analysis of the requirements of specific user groups has been defined: the different users can be divided into clinicians (cardiac surgeons, cardiologists, nurses...) and patients. Each group has its specific requirements regarding information which might be obtained from the SensorART platform.

For biosensors, an extensive work of fabrication by micro technology has been done, followed by testing of sensitivity and reproducibility on cytokines.

A collaboration for detection of specific markers on human blood has been established among HONIG, CNR and UCBL, in order to define the clinical relevance of selected biosensors.

On TET, general requirements have been evaluated. Many actors are currently active in the wireless powering competitive arena, and some of them are coming to the market with commercial solutions. However, at present, none of these systems is suitable for the SensorArt platform. Nevertheless, a constant monitoring of new developments, both in the research field and in the market, is a priority for the consortium. Inductive coupling is at this moment considered the most reliable way of transferring energy trough the skin. The design of a TET for a VAD system is a fine compromise between high power transfer and patient safety. In fact, the system should comply with the norms that regulate the exposure of the human body to the electromagnetic radiation. Another critical point is the coil alignment. TET systems are quite sensitive to misalignment: mechanisms to compensate this effect are under investigation.

Two sets of sensors, both implantable and wearable, have been selected and their implementation is ongoing. It is important to underline that pressure and flow feedbacks are considered crucial by the medical arena to monitor the VAD operation. The possibility of interconnecting the sensors wirelessly in a star network have been studied both for the implanted and wearable nodes.

A simulation station (EndoVascular Evaluator, EVE simulator by Fain Biomedical) has been assembled by SSSA for testing the “sensorized” Synergy pump (Circulite) in different conditions, by implementing the cardiovascular circulatory system of the simulator with different sensors and actuators. The station allows the evaluation of autoregulation unit, when working as data acquisition station as well as VAD controller.

Furthermore, various approaches and technologies for sensors interoperability have been investigated. In line with the Continua Health Alliance guidelines, effort was concentrated on the Bluetooth technology and the Health Device Profile (HDP)/IEEE-11073, which are new application standards that define the requirements for qualified Bluetooth Healthcare and Fitness device implementation and utilization.

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The project consortium

The consortium consists of 13 partners – 4 research centres, 4 universities, 3 SMEs, and 2 large enterprises - from 10 European countries. The project coordinator is Maria Giovanna Trivella, from CNR Consiglio Nazionale delle Ricerche (Italy).

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	Katholieke Universiteit Leuven (Belgium) *www.kuleuven.be*
	Azienda Ospedaliera Ospedale Niguarda Ca' Granda (Italy) *www.ospedaleniguarda.it*
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Project details

SensorART: A remote controlled Sensorized ARTificial heart enabling patient empowerment and new therapy approaches

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