



ULTRAsponder

In vivo Ultrasonic Transponder System for Biomedical Applications

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¹ R = Report, P = Prototype, D = Demonstrator, O = Other

² PU = Public, PP = Restricted to other programme participants (including the Commission Services), RE = Restricted to a group specified by the consortium (including the Commission Services), CO = Confidential, only for the members of the consortium (including the Commission Services)

Revision history

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Executive summary

ULTRAsponder is a project aimed at developing wireless systems for monitoring blood pressure, oxygen saturation, cardiac dimensions, function and rhythm inside the human body.

One of ULTRAsponders objectives is to place wireless sensors (transponders) within the human heart to monitor changes in cardiac function due to heart failure. The transponders will measure and further communicate the results using acoustic waves (ultrasound) to a control unit placed on the skin of a patient. The control unit will be placed in a suitable location, most likely in region(s) of the patients' thorax. The transponders should use minimal power and have the smallest possible physical dimensions. The specifications of the transponders will be given in the following.

This document provides the user requirements of the ULTRAsponder system. There are a great number of possible applications all with its specific set of user requirements. Consequently the user requirements are a multidimensional space with variable dimensions and ranges.

The specifications can be derived in a top down approach starting from the user requirements, and are then called "derivative requirements". From the above it is clear that these derivative requirements greatly depend on the selected application. We will select that application which derivative requirements can be met by the bottom up system specifications.

1 Introduction

Figure 1.1 gives an overview of the complete system.

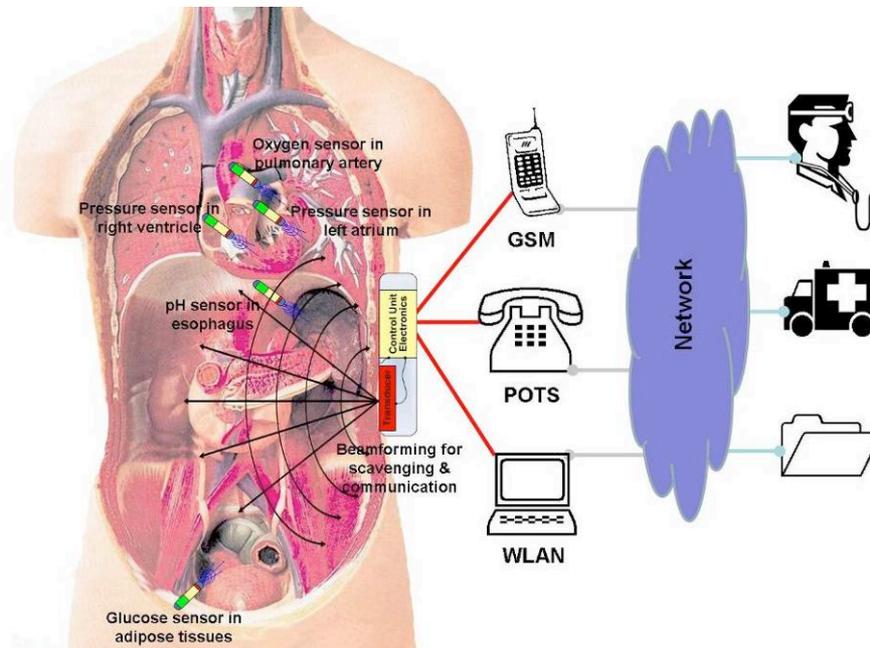


Figure 1.1. ULTRAsponder system overview

The control unit secured to the patient's skin is able to energise and to communicate with a network composed of various sensors embedded inside the transponders and implanted inside the body at a variety of locations: a blood pressure sensor in the right ventricle and in the left atrium, an oxygen sensor in the pulmonary artery, a pH sensor in the esophagus and a glucose sensor in the adipose tissues. The control unit records physiological parameters measured by the sensors, possibly operates a coarse data fusion, and relays data outside the patient's environment e.g. to healthcare providers through standard communication systems.

The transponders will perform a relatively simple task. On demands of the control unit, they will power up, start sensing and communicate the obtained data to the control unit. The transponder will be wireless and without the need for an antenna.

Figure 1.2 shows the intended transponder architecture

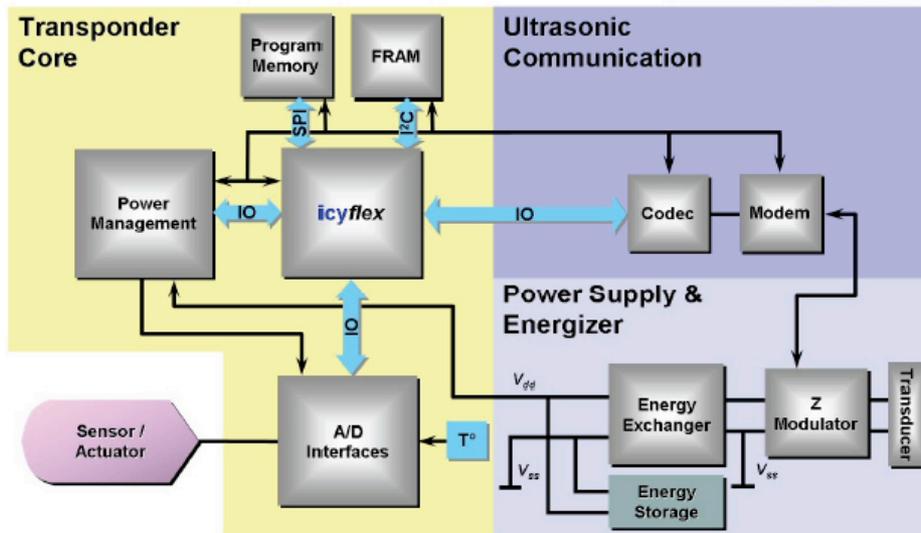


Figure 1.2. Transponder architecture

The transponder must contain the appropriate sensor, transducer and modulator, an energy exchanger converting acoustic into electrical energy to power the electronics, a very low powered digital signal processor with necessary memory- and control units, and the necessary interfaces.

2 Possible applications

2.1 Patients suffering from chronic diseases.

Regular monitoring of Atrial Fibrillation (AF) is required to ensure control of the heart rate.

Hypertension is another cardiovascular disease and the proposed intelligent implantable ultrasonic transponder system would enable physicians to monitor patients with high blood pressure during their normal day life.

An accurate and easily repeated method to follow serial hemodynamic parameters based on pressure recordings could be useful in assessing response to therapy and prognosis in idiopathic pulmonary arterial hypertension (IPAH).

Permanent availability of intravascular pressure opens diagnostic and therapeutic possibilities in hypertension diseases . Furthermore, pressures are related to a long-term outcome of therapy.

Diabetes mellitus is a well-known chronic disease resulting in several end-organ complications. Here a transponder would enable the networking of an implanted glucose sensor, not only to monitor patient glucose levels, but also to incorporate the sensor into a “closed feedback loop” system for insulin delivery.

More generally, this smart transponder would enable monitoring of the patients’ response to therapy.

Pressure recordings provide data related to haemodynamic changes due to an increased volume load. Such data provide useful information for tailoring an optimal diuretic dose in patients suffering from congestive heart failure.

Implantable sensors capable of monitoring haemodynamic changes like absolute right ventricular pressure and mixed venous oxygen saturation over extended periods of time may reveal to be most useful for patients with heart failure. Studies of titration of vasodilator dosage according to haemodynamic end-points have demonstrated important clinical improvements that may not have been possible when simply using an empirical target dose.

2.2 Hospital patients.

At present, hospitalised patients are monitored intermittently, intensively or continuously (e.g. intensive care units). This monitoring consists in vital sign measurements (blood pressure, heart rate, ECG, respiratory rate and temperature), visual appearance and verbal response

Patients undergoing surgery require monitoring levels ranging from very high during and immediately after surgery, to intermittent during the post operative recovery period. The automation of this process is desirable not only for the healthcare provider but also for the patient.

2.3 Elderly patients.

Monitoring in a minimally invasive manner this aging population in their domestic environment is very important especially during months of non-temperate weather (either very cold or very hot). This would allow earlier detection of any degradation in their condition. When correlated with physiological vital sign measurements, this system clearly has the potential to identify those persons being most exposed to potentially life-threatening risks.

2.4 Other

Ambulatory direct Left Atrial Pressure (LAP) monitoring may detect dynamic ischemia and help to confirm successful revascularization.

Mixed venous oxygen saturation (SvO₂) measured in the pulmonary artery could be used for diagnostic decisions, therapeutic guidance, prognostics and, in combination with oxygen uptake and arterial oxygen saturation to determine the cardiac output according to Fick .

The pH is measured to diagnose Gastro Esophageal Reflux Disease or GERD.

Biosensors are of great interest for their ability to monitor clinically important analytes such as blood gases, electrolytes, and metabolites.

A study demonstrates that higher concentrations of Nitric Oxide (NO) (measured with a real time-sensor in or around the facet joints) in the perifacetal region in chronic low back patients compared with healthy controls indicate that the degenerative process of the joints in these patients may cause increased NO production.

Enhance the quality of life of these populations at risk is another goal of the project; it is proven that early diagnosis and treatment prevent long-term complications.

3 User requirements

The user requirements depend to a great extent on the application (see previous chapter). This means that care has to be taken in the interpretation of the user requirements given in the text below (in particular sections 3.1 and 3.2), they can be different for other applications. Nevertheless they can serve as a guide for the technology and prototype development.

3.1 Localization

For one possible application, the sensors shall be placed intramurally in septum of the right and left ventricle and in the lateral free wall of the left ventricle (see figure 3.1).

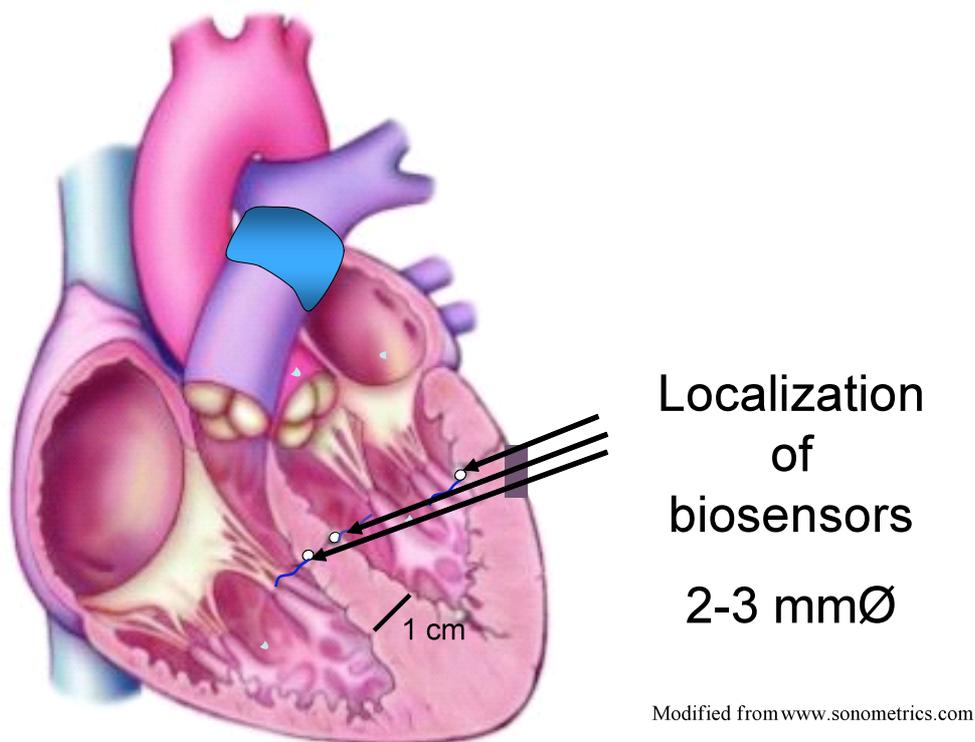


Figure 1.3. Biosensors localizations in the human heart

3.2 Physical dimensions

For this particular application it is recommended that the transponders dimension should correspond to a cylinder with a maximum diameter of 2-3 mm and a maximum length of 5 mm. This maximum size must be satisfied when used in humans. The transponders used for testing (see experimental study below) can be slightly larger, 5-7 mm in diameter and a length of 10 mm. However the demonstrator in the present project will have a volume of 2cm^3 . Further industrial versions, requiring significant development (outside the scope of the project) could reach a target volume in the range of 10 to 100mm^3 .

The transponders shall be attached to the endocardium for example with a screw-in-technique as used in pacemaker / ICD leads. This is routinely done in the apex and the septum of the right

ventricle in pacemaker / ICD lead implantations. The lateral free wall of the right ventricle and also the left ventricle might be too thin for this technique and the risk of penetration of the ventricular wall is high. Minor damaging techniques should be used for these localizations.



Figure 3.2. Sensors' fixing screws.

Screw in technique used for attaching pacemaker leads to the septal endocardium in the right ventricle and atrium (see figure 3.2)

3.3 Functional description

3.3.1 Pressure

The transponders should be able to measure intra cardiac pressure. With three transponders, two placed in the left ventricle and one in the right ventricle, complete cardiac pressure monitoring is possible.

3.3.2 Oxygen saturation

Oxygen saturation should be measured in the right ventricle. Together with simple finger measured O₂-saturation levels, the situation of oxygen supply and oxygen demand can be monitored and be helpful in diagnostic and therapeutic decisions.

3.3.3 Frequency of use and duration of operation

Pressure, oxygen level and cardiac dimensions should be measured once daily. The duration of the measurements should be long enough to ensure good quality. Furthermore, rapid changes in pressures and dimensions could indicate myocardial ischemia and should be recorded. ECG should be measured once daily for 5-10 seconds. In addition, there should be a rate dependent onset of registration. When heart rate exceeds 150, date and time for this event should be recorded and the ECG for at least 2-3 of these episodes should be saved. The ECG for each episode should be of 5-10 seconds duration.

3.3.4 Dimensions

The transponders should be able to communicate with each other and monitor the dimensions between them. An increase in dimension between the transponder in the myocardial septum and the lateral free wall of the left ventricle may indicate a worsening of heart failure with left ventricular overload. Similarly, an increase in right ventricular dimensions could indicate rise in pulmonary pressures. A decrease of right ventricular dimension could indicate overuse of diuretics and medication adjustment can be necessary. In addition, cardiac output and myocardial shortening fraction function can be calculated from dimensions monitoring.

3.3.5 ECG

Patients with heart failure have increased mortality. Mortality is partly due to deterioration of cardiac function. However, a substantial proportion of deaths in heart failure are sudden and caused by cardiac arrhythmias¹. Prediction of sudden death is a main problem in patients with heart failure. Current guidelines for risk stratification are insufficient and further monitoring and diagnostic techniques are required [2-4]. It is generally accepted that heart failure patients with non sustained ventricular tachycardia (nsVT) on Holter monitoring (ECG recorded for 24 hours) are at high risk of sudden death. In these patients implantation of an internal cardiac defibrillator (ICD) should be considered. However, a single 24 hour ECG registration is far from informative of what heart rhythm these patients have the rest of the time. Continuous monitoring of heart rhythm can improve risk stratification and selection of the patients who will benefit from ICD therapy.

3.4 Safety

It is of most importance that the devices, when first attached, do not release, since it will have fatal consequences if the transponders are let loose into the bloodstream. A loose device in the right ventricle will follow the bloodstream into the pulmonary arteries and pulmonary capillaries. This can cause a pulmonary embolism and pulmonary infarction.

A loose device in the left ventricle can, if loose, follow the bloodstream through the aortic valve and as a fatal consequence cause a cerebral ischemic stroke.

3.4.1 Thrombosis and bleeding

Antithrombotic therapy is not routinely recommended for devices placed in the right ventricle e.g. pacemaker leads. For devices in the left ventricle however, full anticoagulation therapy is recommended (e.g. mechanical valve replacement). Therefore, transponder implantation in the left ventricle should be accompanied by full anticoagulation i.e. use of Warfarin with INR levels of 2.5. INR level must be monitored thoroughly. A substantial proportion of heart failure patients meet indications for anticoagulation therapy due to their heart failure and will be at anticoagulation therapy at the implantation occasion. At implantation, therefore, INR should be below 2 to minimize bleeding complications. Patients who are treated with acetylsalicylic acid (ASA) and Plavix due to coronary stent implant should continue this medication during transponder implantation. INR levels for patients on ASA and Plavix must be between 2 - 2,5.

3.4.2 Penetration and tamponade

All kind of instrumentation of the right (and left) ventricle, includes a potentially risk of penetration with consequent tamponade. Tamponade is defined as blood leakage into the pericardial sac with elevation of external pressure around the right (and left) atrium and ventricle. This can lead to life-threatening decrease in cardiac output. These patients must be carefully monitored peri- and postoperatively in 24 hours with respect to symptoms of cardiac tamponade. If signs of cardiac tamponade develop, echocardiographic examination should be performed immediately. Echocardiographic examination can confirm liquid in the pericardial sac. Pericardial drainage should be performed if necessary.

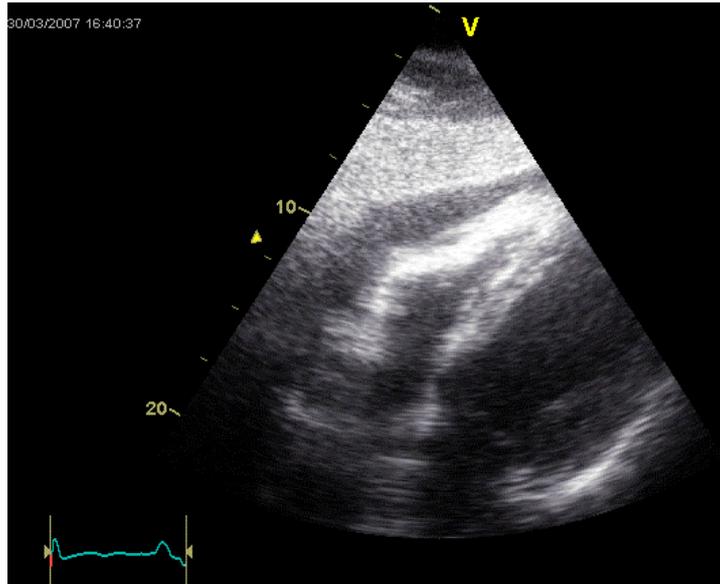


Figure 3.3. Blood in the pericardial sac after penetration of the right ventricle.

3.4.3 Infection

All intracardiac procedures should be accompanied by antibiotic prophylaxis. Standard prophylaxis may be i.v. Cefalotin 1g x3 with first dosis one hour before start of procedure, followed by two doses with 6 hours interval.

4 Conclusion

This document provides the user requirements of the ULTRAsponder system. There are a great number of possible applications all with its specific set of user requirements. Consequently the user requirements are a multidimensional space with variable dimensions and ranges.

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