Packaging of implantable accelerometers to monitor epicardial and endocardial wall motion.

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Abstract

Acceleration signals, collected from the inner and the outer heart wall, offer a mean of assessing cardiac function during surgery. Accelerometric measurements can also provide detailed insights into myocardial motion during exploratory investigations. Two different implantable accelerometers to respectively record endocardial and epicardial vibrations, have been developed by packaging a commercially available capacitive transducer. The same coating materials have been deposited on the two devices to ensure biocompatibility of the implants: Parylene-C, medical epoxy and Polydimethylsiloxane (PDMS). The different position-specific requirements resulted in two very dissimilar sensor assemblies. The endocardial accelerometer, that measures accelerations from the inner surface of the heart during acute animal tests, is a 2 mm-radius hemisphere fixed on a polymethyl methacrylate (PMMA) rod to be inserted through the heart wall. The epicardial accelerometer, that monitors the motion of the outer surface of the heart, is a three-legged structure with a stretchable polytetrafluoroethylene (PTFE) reinforcement. This device can follow the continuous motion of the myocardium (the muscular tissue of the heart) during the cardiac cycle, without hindering its natural movement. Leakage currents lower than 1 μ A have been measured during two weeks of continuous operation in saline. Both transducers have been used, during animal tests, to simultaneously record and compare acceleration signals from corresponding locations on the inner and the outer heart wall of a female sheep.

Keywords: *accelerometer, heart motion, packaging, endocardial, epicardial, biocompatibility.*

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1. Introduction

Monitoring of the cardiac motion is desired in a number of applications. 2D-, 3D- and Doppler-echocardiography (Mandinov et al. 2000; Zamorano et al. 2009; Tang et al. 2016), together with cardiac MRI by myocardial tissue tagging (Shehata et al. 2009; Wu et al. 2014), are the imaging modalities of choice for clinical evaluation of both global and regional myocardial function. Despite them being non-invasive, fast and widely available, the accuracy of these measurements is limited by image and signal quality. Furthermore, it is not straight forward to obtain information about the movement of the myocardium in all three dimensions (Abraham and Nishimura 2001).

During surgery, an invasive alternative to imaging techniques is offered by catheters inserted in the heart cavity, directly monitoring the pressure in relation to the volumetric changes of the muscle. The dp/dt max, the maximum time derivative of left ventricular pressure signal, is routinely considered a reasonable index of myocardial contractility. (Sarazan et al. 2011; Norton et al. 2009; Markert et al. 2009). All the mentioned techniques can only offer instantaneous recording of cardiac function and lack the possibility of a long term assessment of the ventricular function.

Over the years there has been a growing interest towards the development of implantable accelerometers that directly measure the mechanical vibrations generated from the rhythmic contractions of the heart. The use of micromachined sensors offers the advantages of small form factor, low power consumption and higher accuracy and sensitivity in all relevant directions. Already in 1993, Padmanabhan et al. successfully recorded heart sounds with a MEMS piezoelectric accelerometer placed on the patient's chest. Wood et al. (1994) measured cardiac vibrations by means of an analog uniaxial accelerometer (Entran EGA-125-50-D) cemented in aluminum and glued to the epicardium by means of cyanoacrylate glue. Rickards et al. (1996) were the first to sample the endocardial acceleration, by embedding a unidirectional accelerometer in the tip of a standard pacing lead. A good correlation has been demonstrated between the measured cardiac acceleration signal and myocardial contractility both for endocardial (Rickards et al. 1996; Theres et al. 2004; Marcelli et al. 2006) and epicardial acceleration (Plicchi et al. 2003; Marcelli et al. 2005).

Some authors suggested the use of cardiac accelerometers to continuously monitor the heart function during cardiac surgery and to identify graft occlusion immediately after coronary surgery (Halvorsen et al. 2008; Fleischer et al. 2008) and others even suggest their use as chronically implantable devices to monitor high-risk patients (Theres et al. 2004) or for rate responsive pacemakers and cardiac resynchronization therapy (Plicchi et al. 2006; Bernal et al 2010; Mansourati et al. 2014).

The myocardial function of patients with an implanted ventricle assist device (VAD), can improve to such an extent that allows explantation of the pump. Implanted accelerometers can be useful instruments to monitor this recovery of myocardial contractility (Grymyr et al. 2015).

Besides cardiac monitoring, a complete and detailed mapping of the acceleration across the heart wall is desirable for experimental investigation. The rhythmic contraction of the heart produces mechanical energy that can be collected by an *in-vivo* harvester and used to power biomedical implants (Zurbuchen et al. 2013). An implantable accelerometer can provide the

knowledge necessary to optimize the design and the placement of such mechanical harvesters.

This work presents two implantable sensors. The first is an exploratory device intended to measure the endocardial acceleration only during acute animal experiments. Such a device can provide detailed mapping of amplitude and frequency components of the acceleration signal across the inner heart wall. The transducer was first presented in Brancato et al. 2015. The present article reports in higher detail the assembly and packaging of the device and its validation, both in-vitro and in-vivo. Moreover, it describes its use in combination with an epicardial accelerometer for mapping heart motion in all locations on the cardiac muscle. This second device, to be stitched on the outer heart wall, was developed to monitor epicardial acceleration during open chest surgery. Although the same coating materials were employed, the sensors' assembly and packaging were tailored to the specific placement of the devices.

The combined use of the two transducers allows for the first time an accurate, and high resolution three-dimensional mapping of cardiac acceleration both on the inner and the outer wall. The epicardial sensor also enables continuous monitoring of heart function, and poses the basis for development of a long term implantable, stand-alone device.

2. Devices assembly and packaging

Most of the literature available on cardiac accelerometers is focussed on validating the acceleration signal as an index of myocardial contractility and on processing the recorded data for different purposes.

Few papers explicitly describe the packaging of the device. Some authors report cementing the transducer in a metal cylinder and glueing it to the heart wall by means of cyanoacrylate adhesives (Wood et al. 1994; Marcelli et al. 2005). While this represents a suitable solution for short term implantation, and an effective way to ensure protection of the electronic, glueing of such a rigid encapsulation is likely to constrain the movement of the underlying tissue. On the other hand, a stable and reliable fixation mechanism that limits the self-motion of the sensor is required to obtain trustworthy measurements and high signal to noise ratios (Theres et al. 2004).

Imenes et al. (2007) proposed a soft PDMS encapsulation for their epicardial accelerometer. They tested two different silicones: Elastosil R Plus 4001/40 (Wacker Chemie AG) and MED-6015 (NuSil Technology). A reliable fixation was obtained by stitching the packaged device (14.50 x 11 x 5.20 mm) to the heart wall, but the stress generated during myocardial contraction caused the sutures to cut either through the silicones or the heart tissue, making it unsuitable for chronic implants.

This work presents the encapsulation of a commercially available 3-axis accelerometer (BMA 280, Bosch Sensortec). The same sensor was used for both the endocardial and the epicardial devices. The BMA 280 is a capacitive transducer with an integrated analog-to-digital interface. Four different acceleration ranges are available: $\pm 2g$, $\pm 4g$, $\pm 8g$, $\pm 16g$. The $\pm 2g$ range was deemed sufficient for this application. The device offers the advantage of a small form factor (2 x 2 x 0.95 mm), an excellent resolution (0.244 mg) and a high sensitivity (4096 LSB/g). The current consumption at 3.3V is only 130 μA but, when high sampling rates are not required, it can further be decreased to 6.5 μA by placing the device in low power mode.

The selected accelerometer is factory calibrated and has very low temperature coefficients of sensitivity and offset: respectively 0.015%/°C and 1 mg/°C. As temperature in the human body is regulated in within few degrees Celsius, it will not introduce significant errors in the measurement.

Slow baseline drift along the three axes is corrected by an on-chip high pass filter that also removes the DC component, representative of the device orientation.

The accelerometers were soldered on small circular printed circuit boards (PCB), with a diameter of 3.2 mm (Fig. 1). Four vias provide electrical connection between the pads of accelerometer and the back of the PCB. Four polyurethane insulated copper wires, each with a diameter of 150 μm were soldered to the PCB. To ensure biocompatibility of the cable, a 6 μm thick medical grade heat shrinkable tube (103-0521, Vention medical) was applied around the wires.

Fig. 1 Implantable accelerometers' printed circuit board: **a** bottom layer; **b** top layer; **c** sensor mounted on the board

2.1. Endocardial accelerometer

The endocardial sensor is designed to be pushed through a puncture in the heart wall during terminal animal experiments. The device consists of a soft saucer-shaped head mounted on a rigid pusher rod.

The assembly procedure consists of three distinctive steps: packaging of the sensor, fabrication of a sealing lip, attachment of the pusher rod (Fig 2).

Fig. 2 Endocardial accelerometer: **a** exploded view; **b** 3D view¹

At first the accelerometer board described in the previous section was coated with three successive polymeric layers. To provide good electrical

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insulation to the electronic components, they were coated by a conformal film of parylene-C with a thickness of 5 μm . Parylenes are poly(p-xylylene) polymers deposited from a gas phase through chemical vapor deposition (CVD). This ensures that a continuous pinhole-free layer is applied on every exposed surface of the device. Thanks to its outstanding chemical resistance and low water vapor permeability, parylene-C is a supreme barrier against the diffusion of moisture and biological fluids in the implant. To provide mechanical support to the accelerometer and its soldering joints, a drop of medical epoxy (EPO-TEK 302-3M) was used to glob top the sensor.

As a last coating, the device was embedded in a hemisphere of low-viscosity, medical grade PDMS (NUSIL MED-6015). To ensure proper bonding of the PDMS, the PCB was dipped in a primer (NUSIL MED1-161) and allowed to dry for 30 minutes at room temperature. The base polymer of the PDMS and its curing agent were thoroughly mixed and degassed for 15 minutes in a pulsating vacuum to remove air bubbles. A two-part milled polyvinyl chloride (PVC) mould (Fig. 3) was fabricated to cast PDMS on five sensors at a time. The accelerometer boards were placed in the bottom half of the mould, while the silicone mixture was poured in the upper half. The two parts were pressed together and placed in an oven at 100 $^{\circ}\text{C}$ for 4 hours until complete crosslinking of the polymer.

Fig. 3 PVC mould to cast PDMS: five accelerometers are shown, separated by four threaded holes for assembly of the mould.

Secondly, the sealing lip was fabricated. An 800 μm thick film was obtained by spin-coating PDMS over a silicon wafer and baking it on a hot-plate at 150 $^{\circ}\text{C}$ for 15 minutes. The film was peeled off from the wafer and small PDMS disks with a diameter of 8 mm were cut out. Using a medical grade one-component silicone adhesive (Nusil MED-1000), a disk was bonded on the back of each sensor thus resulting in a saucer shaped sensing “head”.

Thirdly, a PMMA U-profile is attached on the back of the device, enclosing the four lead wires. This rigid shaft is used to push the sensor through a small opening in the heart wall (Fig. 4a). During fabrication, the groove in the PMMA rod is aligned with the positive y-axis of the accelerometer. Therefore, during surgery, it can be used as a reference to orientate the transducer along the cardiac coordinate system. Small notches, evenly spaced by 3 mm, are carved in each pusher rod. Before implantation, the rod

can be broken along these score lines, making it adjustable to different heart wall thicknesses.

The sealing lip folds back during insertion and snaps open in the cardiac cavity. Hence, the transducer is secured on the epicardium despite the opposing intracardiac pressure, and bleeding from the insertion hole is blocked by the sealing lip. After insertion of the endocardial accelerometer a laser-cut PMMA ring is slid over the pusher rod locking the sensor firmly to the inner wall (Fig. 4b).

Fig. 4 Schematic views of the endocardial accelerometer: **a** insertion through the heart wall; **b** fixation with a PMMA ring

The fixation mechanism allows the device to follow the heart wall motion without hampering it. When contracting, the ventricular myocardium undergoes thickness changes. During systole the PMMA ring can slide over the pushing rod, accommodating for radial thickening. The small diastolic pressure exerted from the blood is enough to keep the sensor anchored on the epicardium and prevent it from drifting inwards during relaxation.

2.2. Epicardial accelerometer

As the endocardial, the epicardial accelerometer described in this section can serve as an exploratory device to study the heart wall motion in acute animal tests. However, the much less invasive implantation technique, also makes it suitable for monitoring purposes during open chest surgery.

Particular care was taken to find a reliable fixation technique that ensures secure anchoring of the sensor to the epicardium. For the device to minimally interfere with the physiological contractions of the heart, a fixation technique is required to allow its free, unconstrained movement. Although offering a trustworthy connection, stitching of a rigid structure has been reported to induce high local stresses on the epicardium that can cause the sutures to cut through the device's encapsulation or the heart tissue (Imenes et al. 2007).

For this reason, the epicardial accelerometer was designed as a three-legged stretchable structure able to conform to the natural curvature of the heart, and accommodatingly follow its deformations.

The same packaging materials used for the endocardial accelerometer were employed. First, the sensor's PCB was coated with a layer of 5 μm of Parylene-C. Therefore the board was glued on a 1 mm-thick laser cut PTFE support (Fig. 5a) using medical epoxy (EPOTEK 302-3M) and globe-topped

using the same adhesive. A soft PDMS layer (NUSIL MED-6015) was finally molded around the assembly, using the PMMA mold depicted in Fig.5b.

Fig. 5 **a** PTFE support with three stretchable legs; **b** PMMA mould to coat PDMS on the epicardial accelerometer

The structural flexibility of the wavy PTFE legs, together with the low young modulus of the selected PDMS, allows the assembly to compliantly follow the actual stretch of the cardiac muscle, therefore reducing the stress exerted by the sutures on both the PDMS and the heart tissue. The stitching rings, at the end of each supporting leg, ensure solidity of the implant. Fig.6 schematically illustrates the sensor assembly and its packaging layers.

Fig. 6 Epicardial accelerometer assembly: **a** top view; **b** aligned section view; **c** 3-D drawing

2.2.1. Stretchability of the legs

The transversal section of the epicardial accelerometer's stretchable leg is displayed in Fig. 7a. Both the PDMS and the PTFE backbone contribute to determine the mechanical properties of the structure. PDMS is an elastomer and behaves as a linear elastic material for small deformations. PTFE, or Teflon, is a solid fluorocarbon polymer with high molecular weight. The original length of the stretchable portion of each leg of the substrate is 3 mm. Because of its wavy pattern, however, the fully elongated length of each segment is 6.45 mm, corresponding to 215% of its initial length. A simplified two-spring mechanical model of this assembly is shown in Fig. 7b.

Fig. 7 **a** Transversal section of accelerometer's leg; **b** 2-spring equivalent model

The spring constant of the Teflon meander was estimated using the finite element analysis software Comsol Multiphysics 5.2. A value of 0.4 GPa was used for the Young's modulus of Teflon. Applying a tensile force F , and measuring the maximum resulting displacement x , the spring constant was calculated.

$$k_{PTFE} = \frac{F}{x} = 1.09 \frac{N}{mm}$$

No value is available for the Young's modulus of the selected PDMS (Nusil MED-6015), however, it can be deduced from its durometer hardness value of 50 shore A. Using the following formula, proposed by Gent (1958), we obtain:

$$E_{PDMS} = \frac{0.0981 \times (56 + 7.62336 \times S)}{0.137505 \times (254 - 2.54 \times S)} = 2.45 \text{ MPa}$$

Where S is the hardness of the material and E_{PDMS} is the estimation of the Young's modulus of the PDMS. A maximum longitudinal strain of 20% was measured in the left ventricle (Skulstad et al. 2006) by tissue Doppler imaging techniques. Similar values, of about 15%, are reported for global circumferential strain and global longitudinal strain in the left ventricle (Onishi et al. 2015) with peaks of 28% after exercise (Santoro et al. 2015). In this range, PDMS mechanical behaviour is well approximated by a linear elastic material (Johnston et al. 2014) and therefore the PDMS spring constant for each leg can be calculated as follows:

$$k_{PDMS} = \frac{E_{PDMS} \times A}{l} = 5.51 \frac{N}{mm}$$

Where $A = 9 \text{ mm}^2$ and $l = 4 \text{ mm}$ are, respectively, the transversal area and the length of the PDMS segment undergoing actual stretch.

In conclusion, the spring constant of the silicone encapsulation is five times larger than the one of the PTFE support. Therefore, the stiffness of the structure will be mostly determined by the PDMS matrix. Adding a highly stretchable Teflon support to the device's legs, allows to take advantage of the high stretchability and low young modulus of the elastomer and solves the problem of the sutures cutting through the packaging layer.

3. Measuring system

A measuring system to collect the accelerometers' data was designed and fabricated. The system (Fig. 8) consists of two modules connected through a wireless link. On one end, a battery powered board records signals from several accelerometers and an electrocardiography (ECG) acquisition module. At the other end of the telemetric link, a second board, connected to a personal computer, allows storage and live visualization of the data.

Fig. 8 Block diagram of the measuring instrumentation

Four accelerometers can be attached to the readout board using wires up to 1 m long. The endocardial and the epicardial sensors are based on the same transducer. Therefore, all sensors can be read out identically via a shared I²C bus.

The wireless link offers a practical alternative to the use of long cables that limit the freedom of movement of the medical staff during surgery. Moreover, it ensures a galvanic insulation between the patient and the high-voltage electronics connected to the mains, preventing electrical hazards.

The core of the readout board is a Texas Instruments CC430F5137 microcontroller. This microcontroller was selected for the task due to its compact size, large amount of I/O pins that can be reconfigured at run-time, wide range of peripherals and serial communication protocols and low-power operation. All sensors are read out at a sample rate of 500 Hz, the data is then divided into wireless 32-byte packages and sent to the receiver. The computer board has a similar hardware design, but its software is adapted to transfer the received wireless data over USB.

The main requirements for the wireless link between the two boards are high bandwidth and data-rate, low packet loss and efficient operation. For this purpose, the Nordic nRF24L01+ transceiver module was selected and is operated using SPI on the microcontrollers. The bandwidth of 2 Mbit/s is sufficient to transmit data from multiple sensors at high data rates, while the built-in authentication protocol ensures safety and automatic resending of lost or corrupted data.

To optimize the power consumption of the readout board, the wireless link is designed as unidirectional, only transmitting data from the sensors to the computer board. This greatly simplifies the software requirements and minimizes the chance of losing data packets during communication.

When measuring accelerations from the heart wall, it might be useful to synchronize the data to biological signals recorded from other medical instrumentation. For this reason, the readout board was expanded with the ADS1292 (Texas Instruments), a bio-potential measurement unit that records the electrocardiographic signal and transmits it to the microcontroller over SPI. The actual synchronization with other ECG signals is performed

in post-processing by comparing the waveforms and the exact timing of their R peaks in the QRS complexes.

4. Devices validation

The biocompatible encapsulation proposed for the accelerometers serves a double purpose. On the one hand, it acts as a barrier against diffusion of humidity and ensures protection of the electronics from the aggressive chemical environment of the body. On the other hand, the packaging minimizes the response of the body to the introduction of the implant.

The selected materials are bioinert, they are non-toxic and upon implantation the only expected body reaction is the formation of a collagen capsule around the device. However, the biotolerability of an implant does not exclusively depend on the biocompatibility of its packaging materials. In the design of an encapsulation for an active implantable device a major concern is the electrical current that can leak through the encapsulation. The maximum limit for this leakage current in direct cardiac applications is fixed by the IEC 60601-1 standards at 10 μA .

4.1. In-vitro testing

To prove the functionality of the devices in a wet environment, the first test performed was a soak test. In order to mimic *in-vitro* the electrical properties of the body, a saline solution was prepared by dissolving 0.9 wt% NaCl in water. Both accelerometers were submerged for fourteen days in a bath of the solution held at 37°C, and the acceleration data was streamed to a computer. The devices remained functional, and stable signals were measured throughout the test. During the same timespan the leakage current was measured using the setup schematically depicted in Fig. 9.

Fig. 9 Leakage current measurement setup

All four leads of the sensors were connected together and the current flowing through the saline solution and a submerged platinum electrode was measured using a sourcemeter (Keithley 2450).

The same device was used to generate the excitation voltage. A square wave with a peak amplitude of 3.3 V and period 2 s was chosen, to prevent charge accumulation at the interface electrode/solution from affecting the

measurement. Fig 10 shows the leakage current measured for both accelerometers. The maximum current, after fourteen days of testing, was about 1 μA , ten times lower than the maximum allowable limit (I_{IEC}).

Fig. 10 Leakage current measured from endocardial (continuous line) and epicardial (dashed line) accelerometers

4.2. Animal study: acute experiments

The endocardial and the epicardial accelerometers were used to record the acceleration from the heart wall of a ewe (Swifter-Charolais) during acute animal experiments. The two sensors were implanted close together to identify any discrepancies between the signals recorded from the epicardium and the endocardium.

The study described in this section was approved by the KU Leuven animal ethics committee (P228/2014). The animal received humane care in compliance with the 'Principles of Laboratory Animal Care' formulated by the National Society for Medical Research and the 'Guide for the Care and Use of Laboratory Animals' prepared by the Institute of Laboratory Animal Resources (National Institutes of Health). The sheep was sedated with an injection of ketamine (15 mg/kg) and therefore underwent inhalation induction of anaesthesia with isoflurane gas. A volume-controlled respirator (Dräger, Julian) was used to mechanically ventilate the animal upon intubation and to maintain anaesthesia. Isoflurane (2-3%) in a gas mixture consisting of 80-100% oxygen and room air was employed. Several vital parameters were recorded throughout the experiment: end tidal CO_2 , ECG, heart rate, blood O_2 saturation, arterial and venous flow and pressure.

At first the pressure monitoring catheters were positioned in the left carotid artery and jugular vein. Therefore the ruminant was turned to a supine position to perform a sternotomy. A suitable field for operation was obtained with an epicardial cradle, and all other sensors to monitor cardiac pressure and arterial flow were inserted.

The endocardial accelerometer (Fig. 11a) was inserted first. A purse suture was prepared in the right ventricular free wall and the myocardium was punctured at the centre of the suture using a Cystofix needle ($\varnothing$ 3,5 mm). The device was pushed through the opening, and pulled back to prevent bleeding through the insertion hole. The accelerometer was aligned to the cardiac axis using the groove in the pusher rod as a reference and the purse suture was therefore tightened. The PMMA ring was slid over the pusher rod and fixed with two stitches (Prolene 5/0 RB-2).

The implantation procedure for the epicardial accelerometer (Fig. 11b) is less invasive and more straightforward. Using an alignment mark provided on the Teflon backbone, the device was properly oriented and therefore sutured to the heart wall with three stitches, in close proximity of the endocardial accelerometer (Fig. 11c).

Data was recorded from both accelerometers, together with echocardiographic records (Vivid 7, GE), displayed in real-time during the experiment and stored digitally for post-processing.

Fig. 11 **a** Endocardial accelerometer; **b** epicardial accelerometer; **c** both devices implanted on a ewe's heart

Data sets were analysed using MATLAB (Mathworks, Natick, MA). Fig. 12 shows a 4-seconds window of the baseline signal recorded from the two devices. The acceleration along each sensitive axis of the devices is displayed: X, Y and Z, respectively corresponding to the circumferential, longitudinal and radial axes of the cardiac coordinate system. The signals have been high-pass filtered (cut-off frequency 0.1 Hz) to remove gravitational acceleration and the 50 Hz noise component was also attenuated by a notch filter. The spectral composition of the signals was also estimated by fast Fourier transform (FFT) computation.

Fig. 12 Four seconds of the recorded endocardial and epicardial accelerations in the time and frequency domain

The recorded waveforms correspond well with the epicardial acceleration measured by Halvorsen et al. 2008 along the circumferential axis. A main peak is recorded on each axis that relates to the ventricular depolarization. Minor spikes, caused by the mechanical vibrations generated from aortic valve closure and mitral valve opening, are also visible. The peak-to-peak amplitude of the recorded signal (~ 1 g) is also comparable to the values reported by Fleischer et al. 2008 and Halvorsen et al. 2008. The signals obtained from the two devices are noticeably different, both in time and frequency domains. While the amplitude of the oscillations along the longitudinal direction is comparable, the signals recorded from the endocardium in the circumferential and radial directions are generally larger than the ones from the epicardium.

During the cardiac cycle, the inner and the outer heart wall do not translate in a similar way, but undergo geometrical changes dissimilar one another. The discrepancies measured between the acceleration signals can be explained by torsional movements and radial thickening of the ventricle wall that result in an inward displacement of the endocardium.

Other factors could influence the measured signal: the turbulent flow of the blood against the endocardial accelerometer during diastole causes vibrations superimposed to the movement of the myocardium itself. The dissimilar fixation mechanisms of the two assemblies could also affect the recording. While the epicardial is reliably secured to the heart wall with three stitches, the endocardial accelerometer still has some degree of rotational freedom that could result in self-motion of the sensor.

To validate the acquired measurement, the signals recorded from the accelerometers were compared with the echocardiographic records.

The magnitude of the total acceleration was computed in MATLAB from the signals recorded along each axis. The maximum positive peak in the total acceleration was extracted from each heartbeat and averaged over the duration of the test.

The same parameter was measured, by speckle tracking algorithms, from the accelerations obtained from the echocardiographic recordings. This analysis was performed on eight different subjects.

In the linear regression plot in fig. 13a, the peak acceleration measured from the echo is associated to the corresponding value measured by the sensors. Fig. 13b show the Pearson's coefficient of correlation and the p-values calculated for the extracted data sets.

Fig. 13 a Peak accelerations from echo are plotted versus endocardial (yellow, diamonds) and epicardial (blue, triangles) accelerometers recordings; **b** correlation coefficients and p-values for the two data sets.

There is a significant linear correlation between the acceleration registered by echo, and the signal measured from both accelerometers, $R = 0.89$, $p < 0.01$ for the endocardial and $R = 0.97$, $p < 0.001$ for the epicardial. A higher correlation is measured for the epicardial accelerometer, as speckles from the outer wall were tracked during echo image processing. The value of acceleration recorded from both sensors are slightly lower than the corresponding echo signals as the transducers were located closer to the apex and the echo recordings are relative to the ventricular free wall.

5. Discussion

The invasiveness of the endocardial sensor makes it only suitable as an exploratory device during terminal animal experiments. A more tolerable alternative is the introduction by catheterization of a single axis accelerometer fixed by means of a screw on the inner heart wall, or its integration in a pacemaker lead (Theres et al. 2004; Plicchi et al. 2006; Marcelli et al. 2006).

While these solutions are practical for non-terminal studies, or when only a general feedback on the timing of heart contractions is required (e.g. in rate responsive pacing), they are not optimal when a detailed monitoring of the cardiac motion is desired. The use of a three-axis accelerometer gives more freedom in the placement of the device and allows three-dimensional modelling of heart movements. Moreover, despite its invasiveness, the in-

roduction of the sensor is straightforward and allows a precise and trustworthy fixation in the targeted location.

As demonstrated during animal tests, the epicardial sensor in concomitance with the endocardial accelerometer, can be used to obtain a complete and detailed mapping of the acceleration on the cardiac muscle. Using digital processing techniques, it is also possible to identify the components of the signals in the frequency domain. This knowledge is the fundamental prerequisite for opportune design and placement of a mechanical harvester that collects mechanical energy from the vibrations of the heart.

Thanks to the stretchability of its legs, the epicardial sensor can follow the conformational changes undergone by the cardiac muscle during contraction. As a result, no significant stress is exerted by the sutures either on the packaging or on the heart tissue itself. No mechanical failure of the encapsulation was observed after several hours of testing. The Teflon loops, embedded in the soft PDMS packaging, offer an additional reinforcement in such eventuality. The less invasive implantation procedure and the stretchability of the epicardial accelerometer make it usable as a monitoring device during cardiac surgery and a good candidate for chronic implants. For this reason, all components on the readout board have been selected based on their small form factor and their ultra-low power consumption and work is being performed to integrate them in a stand-alone device.

6. Conclusions

Two different sensor assemblies, to measure endocardial and epicardial acceleration, were presented. The same successive coating layers of Parylene-C, medical epoxy and PDMS were used to encapsulate the same 3-axis digital accelerometer. However, the two devices are very unlike. Because of the invasive implantation technique, the endocardial accelerometer, can only serve as an exploratory device during terminal animal tests. The much less invasive epicardial accelerometer, to be stitched on the outer surface of the heart, is suitable to monitor acceleration signals during surgery. Three stretchable legs allow the device to adapt to the curvature of the heart and to follow its deformation during contraction. The devices remained operational for two weeks when submerged in a body mimicking fluid. The insulation layers ensure leakage currents ten times lower than the 10 μA allowed for direct cardiac application. Animal experiments showed the feasibility of collecting real-time acceleration signals from the inner and outer heart wall and to obtain, by digital processing, information on the spectral components of the recorded signals. The signals measured by both the endocardial and the epicardial device showed a strong and significant correlation with the acceleration extracted from echocardiographic records.

Ethical approval: All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. All procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted.

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