A new class of sensors made from completely biodegradable materials is currently emerging as environmentally friendly and biocompatible with the human body.\cite{1–4} These devices improve the efficacy of implantable systems and reduce waste associated with wearable and point-of-care diagnostics. Highly sensitive pressure sensors can measure pulse, arterial waveform, and pulse wave velocity (PWV), which provide important information about cardiac health.\cite{6–8} In this work, we report the development of a single-use biodegradable pressure sensor patch for application in cardiovascular monitoring. The sensors have a very high sensitivity of 0.76 kPa \(^{-1}\) and are capable of distinguishing a weight of 5 mg. Each patch contains an array of sensors to facilitate fast and easy positioning for cardiac health measurements.

Only a single example of biodegradable pressure sensor was reported so far by Luo et al.\cite{14} in which the microfabricated wireless RF pressure sensor consisted of a parallel-plate capacitor filled with air, connected to an inductor coil.\cite{14} Despite its simplicity, this air gap approach suffers from poor sensitivity in the low pressure regime (<10 kPa).\cite{15–17} Instead, the biodegradable and biocompatible pressure sensor described in this work was designed using the microstructured dielectric approach that was previously described by our group.\cite{17–19} The dielectric consists of a thin, regularly microstructured rubber that is highly compressible, which enables the device to have high pressure sensitivity and fast response time, which are required to measure pulse waveforms and produce accurate PWV measurements.

A schematic image of the device is shown in Figure 1a. It consists of a flexible capacitor, with two substrates assembled via lamination. The key element of our material design is the elastic dielectric between the top and bottom electrodes. Poly(glycerol sebacate) (PGS) is a biodegradable elastomer first reported by Wang et al. for tissue engineering applications.\cite{20} It is an excellent candidate for this application in terms of the degradation characteristics, the mechanical properties, and the processing characteristics. The degradation of PGS has been confirmed and characterized in a range of different conditions. It has been approved by the US Food and Drug Administration (FDA) for biomedical use, which reduces the timeline for implementation. Furthermore, both reactants used in the synthesis of PGS (sebacic acid and glycerol) are inexpensive, which is favorable for large-scale and low-cost applications.\cite{21,22} The mechanical properties of PGS can be tuned by controlling various parameters such as the reaction and curing temperature and time. The elongation at break is larger than 260% and the Young’s modulus can be controlled within the range of 0.05–2 MPa, allowing tunable pressure sensor characteristics, i.e., the sensor sensitivity can be adjusted to fit the pressure range of interest for a particular application. In comparison, the modulus of PDMS used in previous reports\cite{23,24} on high sensitivity pressure sensors is ~1 MPa. The similar modulus for PGS ensures similar high-performance sensing characteristics. We show that PGS has minimal viscoelastic response, which enables fast time response and good reproducibility of the devices with cycling. The simple synthesis mechanism allows PGS to be readily molded into structured dielectrics. Figure 1b shows an scanning electron microscope (SEM) image of the microstructured surface of PGS that was fabricated by molding a 2D array of square pyramids into the PGS prepolymer film before the polymer was physically cross-linked. Pyramids are reproduced with high quality even on very thin (<100 µm) and highly flexible PGS sheets. These microstructures allow the PGS dielectric to elastically deform when an external pressure is applied, storing and releasing the energy reversibly, thus minimizing undesirable viscoelastic behavior.\cite{17} For the electrodes, several biocompatible corrotable metals can potentially be selected. Pure Mg, pure Fe, and their alloys have already been in use for more than a decade in clinical trials in applications such as biodegradable stents and bone scaffolds.\cite{23,24} In addition to investigations on dissolution rate, change in electrical properties, chemical properties, and morphology, Mg, Fe, and the common used alloying elements are also being investigated from the point of view of pathophysiology, toxicology, and daily allowance in the body, providing design rules for human safety: in particular Mg and Fe are essential nutrients with a daily allowance of 0.7 g and 10–20 mg, respectively.\cite{25} In previous works, resistor–inductor–capacitor (RLC) resonators made of Mg, Fe, and their alloys were investigated as RF components for wireless biosensor applications.\cite{4} Luo et al. used electodeposited Zn/Fe bilayers as conductor material for their sensor,\cite{14} while Yin et al., investigated the dissolution properties of thin films of Mg, Mg alloy, Zn, Fe, W, and Mo, to assess their potential for use in water-soluble, physically transient electronics.\cite{26} In this project, Mg is used for the top and bottom electrodes due to its easy processing, biocompatibility, and rapid rates of hydrolysis. A thin layer of Fe is used as an adhesion layer to promote good adhesion of Mg with the biodegradable polymer substrate.
The sensitivity of the biodegradable pressure sensor is investigated for a 4 × 5 sensor array, in which the sensor area is defined by the intersection of two orthogonal electrodes (2.42 × 2.42 mm²). The pyramids on the surface of PGS have a height of 2 µm, a pyramid base width of 4 µm, and a spacing between pyramids of 5.6 µm (Figure 1b). Figure 2a shows the pressure response from three sensors. The pressure sensitivity S is defined as the slope of the traces in Figure 2a (\( S = \frac{\delta (\Delta C/C_0)}{\delta p} \)), where \( C \) and \( C_0 \) are the capacitances with and without applied pressure, and \( p \) is the applied pressure. The pressure sensitivity, averaged over 20 sensors, is 0.76 ± 0.14 kPa⁻¹ in low pressure regime (\( p < 2 \) kPa) and 0.11 ± 0.07 kPa⁻¹ at higher pressures (2 < \( p < 10 \) kPa). These values are in good agreement with results previously reported by our group for nonresorbable PDMS-based sensors with a similar design.\(^{17}\) Moreover, these pressure sensitivities are ≈60 times higher (10 < \( p < 20 \) kPa), two orders of magnitude higher (×180, 2 < \( p < 5 \) kPa), and three orders of magnitude higher (×1260, \( p < 2 \) kPa) as compared to previously published biodegradable pressure sensors (0.0006 kPa⁻¹, 0 < \( p < 20 \) kPa).\(^{14}\) Our obtained high sensitivity should enable new applications, especially in the field of cardiovascular monitoring. And for applications where a high sensitivity is required at higher pressures, the design can be adapted with larger pyramids, as described by Tee et al.\(^{27}\) There is non-negligible variability from one sensor to the other within the array, as illustrated by: (i) the standard deviations associated with pressure sensitivities (0.76 ± 0.14 and 0.11 ± 0.07 kPa⁻¹), and (ii) the variations of \( C_0 \) (6.22 ± 2.05 pF) when comparing 20 sensors in the array. However, in the context of cardiovascular monitoring, this variability between sensors is not as critical since the signal of interest is the shape of the pulse wave, which is measured as a relative variation of pressure. Cardiologists are usually more interested in peaks location and relative peak area, together with specific time markers such as the foot of the wave used to calculate the pulse wave velocity (PWV).\(^{7}\) In this work, the differences between sensors can be explained by: (i) slight variations in the thickness of the PGS at different locations in the array, (ii) slight variations in the area of capacitors parallel plates (the metallization lines of top and bottom electrodes are defined with a shadow mask), and (iii) additional air gaps that form between the top electrode and the PGS dielectric. The presence of the air gaps, due to small curvatures in the flexible substrate, was previously confirmed by comparing the experimental results with calculated values.\(^{18}\) In Figure 2a, there is a reduction in sensitivity for pressures \( p > 2 \) kPa. Our current sensor has a favorable sensing response as it shows a progressive damping in sensitivity, which will further extend the range of detectable pressures to higher loads in which high sensitivity is not required, hence resulting in a more versatile pressure sensor.\(^{17}\) The sensitivity and sensing range can easily be adjusted by choosing the appropriate pyramid height and density on the PGS film.\(^{18}\) Another important advantage of using a biodegradable sensor is its ability to be utilized in a controlled manner within a certain area of the body, which can be tailored according to the patient’s needs.
The sensor performance is also investigated while it is bent at various convex curvatures. As illustrated in Figure S4a (Supporting Information), the pressure response is very stable at all bending radii down to 27 mm, which is sufficient in the context of external cardiovascular monitoring (e.g., if the device is attached at the wrist, or on the skin above the femoral or carotid artery). The pressure sensitivity has a slight decrease for applied pressures in the ranges 5–10 and 0.1–2 kPa when maintained at a bending radius of 27 mm (Figure S4b, Supporting Information). This is ≈10% and ≈20% lower, respectively, as compared to operation without any bending. At pressures p > 10 kPa, no significant change in the pressure sensitivity is observed. As previously described, in the context of the present application, such a change in sensitivity is not especially critical, since the signal of interest is the relative variation of pressure over time, i.e., arterial pulse wave shape.\(^7\)

In vitro biodegradation studies are performed to further investigate device resorption characteristics. The objective is to demonstrate that these devices will indeed degrade (if needed) after their period of usage. The mass-loss kinetics of the device, which is composed primarily of the polyhydroxybutyrate/polyhydroxyvalerate (PHB/PHV) top and bottom substrates with metallization layers and PGS dielectric, is shown in Figure 4a. After being immersed for seven weeks in a phosphate-buffered saline (PBS) solution at 37 °C, the pressure sensor weight remains at ≈85% of its initial value. As shown in Figure 4b, the first layer to dissolve is the metal layer (Fe–Mg), in which the degradation occurs as soon as the PBS buffer penetrates into the PHB/PHV bonded substrates. The complete resorption of both PHB/PHV and PGS films requires a duration of at least a few months and depends greatly on its biological environment.\(^{28,29}\) For PGS, Wang et al. have shown that films immersed in a PBS solution at 37 °C lost 17.6% of their dry weight after 60 days.\(^{20}\) The degradation rate was found to be higher in vivo, with surface erosion being typically in the range of 0.2–1.5 mm month\(^{-1}\).\(^{28}\) For PHB/PHV, Pouton and Akhtar have shown that the complete weight loss of a 50 µm thick PHB/PHV film happened after ten weeks in soil at 25 °C, and after 50 weeks in sea water at 15 °C.\(^{30}\)
In the present study, we are also particularly interested in the mechanical properties of the PGS dielectric layer upon degradation in order to understand how well this key element of the sensor would retain its performance after prolonged exposure to humid environments, e.g., during transport or storage. It is also desirable that the elastomer has very limited viscoelastic behavior and hysteresis, even after being exposed to a degrading environment. Figure S5 (Supporting Information) shows stress–strain curves for PGS. It is observed that very little hysteresis is present both in tension and compression regime, even after seven weeks in PBS solution at 37 °C. The tensile modulus and compression modulus of PGS as a function of incubation duration are given in Figure S6 (Supporting Information). It is observed that both moduli decrease when the incubation duration is increased. A simple linear fit indicates a reduction of about 10% and 4% week\(^{-1}\) for the tensile and compression moduli, respectively. Modulus degradation will affect the device performance mainly by changing the

Figure 3. Pressure sensor array performances. a) The sensor array of 4 × 5 pressure-sensitive elements is able to detect the presence of small weights such as a grain of salt with fast time response (weights: 55, 9, and 5 mg). b) Capacitance change distribution on the sensor array upon placing light weights such as a bee (22.5 mg), a grain of rice (21.8 mg), and a bipod object (5 g). The array allows to localize and sense the application of pressures as small as 3 Pa. The measurement with bipod object illustrates the crosstalk effect between several pixels located close-by in the array, which could be minimized in the future by designing stretchable top and bottom electrodes.
output response sensitivity. Additionally, the viscoelasticity of PGS is investigated by relaxation measurements, as illustrated in Figure 4c,d. The measured load curves are evaluated using the modified superposition model of Findley adapted from the Fung model [31,32](Figure 4c). The nonlinear viscoelastic model of Findley was chosen because it is observed in the measurements that the relaxation function depends on the strain level. This nonlinear behavior requires a more general description than the separable quasilinear viscoelasticity theory. [32] In the model of Findley, the relaxation depends on time and strain level as shown below in Equation (1) [31]

\[ F(t,\varepsilon) = F_0(\varepsilon) e^{-B t} \quad (1) \]

where \( F \) is the time and strain-dependent load, \( F_0 \) is the initial load (load immediately measured when the strain is applied), and \( B \) is the relaxation coefficient that describes the strain-dependent rate of load relaxation. The averaged \( B \) and \( F_0 \) for PGS samples as a function of incubation duration are plotted in Figure 4d,e. After seven weeks, a slight decrease is observed for \( F_0 \) (rate ~6% week\(^{-1}\)), while no significant change is observed for \( B \). This observation indicates that for samples evaluated after one week of incubation (under a constant applied strain of 0.05, which corresponds to an applied pressure of 34 kPa), the measured initial load is around 2 N, and it remains at 90% of this initial value after 3 min. After seven weeks of incubation, the measured initial load is around 1.4 N and again it is ~90% of this initial value after 3 min. In conclusion, our in vitro biodegradation study of PGS shows that there is no significant change in the viscoelastic behavior of PGS after seven weeks of incubation in PBS solution. This is attributed to the fact that PGS undergoes surface erosion, in which the main mechanism of degradation is the cleavage of ester linkages. Unlike bulk degradation mechanisms present in most biodegradable polymers, PGS is characterized by a slow loss of mechanical strength relative to mass loss, which is an asset to our present sensor application.

The storage stability is tested for pressure sensors that are stored for one week in the following two conditions: (1) Storage in an oven at a temperature of 45 °C, a large open water container placed in the oven allowing reaching 40% relative humidity and (2) storage in a freezer at a temperature of −6 °C with 56% relative humidity. After 7 d storage, the response characteristics of the pressure sensors are measured and

Figure 4. In vitro degradation of pressure sensor and PGS dielectric layer. a) A plot of mass remaining demonstrates that the biodegradable pressure sensor starts to lose weight already after one week being immersed in phosphate-buffered saline (PBS) solution at 37 °C, the weight being ~85% of its initial value after seven weeks of incubation (study performed on four devices). b) Photographs from a representative device before in vitro degradation and after seven weeks of incubation. The first layer to be dissolved is the metal layer (Fe—Mg). The degradation occurs as soon as the PBS solution penetrates through the PHB/PHV bonded substrates. c) In vitro degradation study of PGS, where the viscoelastic properties are investigated through relaxation tests. The samples were immersed in phosphate buffered saline solution (pH 7.4, Medicago, USA) at 37 °C. The PBS solutions were renewed every week to prevent significant changes of pH. After 1, 2, 3, 4, 5, 6, and 7 weeks, seven PGS cylinders were removed from incubator, washed in deionized water, dried with towel and air jet, and dried in vacuum during 24 h. For each cylinder, a relaxation test was performed at five different strain levels (\( \varepsilon = 0.05–0.25 \)), and the Findley model was used to extract the initial load \( F_0 \) and the relaxation coefficient \( B \) from the measured relaxation curves. d) Relaxation coefficient \( B \) and e) initial load \( F_0 \) as a function of the incubation duration.
compared to characteristics prior storage (see Figure S7, Supporting Information). As shown in Figure S7a,b (Supporting Information), the sensitivities at low and high pressure regime are not affected by the harsh storing conditions, and as illustrated in Figure S7c (Supporting Information), the sensors are still able to successfully measure the wrist pulse wave after one week storage in extreme conditions.

The high sensitivity and fast response time of the sensors make them suitable for cardiovascular monitoring such as arterial tonometry and PWV measurements. A critical, global concern is the prevalence of cardiovascular diseases (CVD), which is the primary cause of premature death in the world today, and hypertension was identified as the main risk factor and leading cause of CVD. The early detection and regular monitoring of hypertension patients improves the prognosis and reduces societal cost. Measurement of carotid-femoral pulse wave velocity (cf-PWV) is currently the “gold standard” to measure aortic arterial stiffness, which is directly correlated to hypertension. Pulse wave velocity is the speed at which the blood pulse wave travels in arteries. In elastic (healthy) arteries, the blood pulse wave travels slowly, while in stiff arteries (arteries tend to become stiffer with increasing age and diseases, e.g., hypertension), the pulse waves will travel faster. Due to its ability to independently predict cardiovascular risk and mortality, cf-PWV measurement is a reference in international cardiology/hypertension treatment guidelines. A major challenge in developing countries is the cost-effective screening of large populations in order to diagnose hypertensive patients early. Having a low-cost single-use biodegradable sensor patch for point-of-care measurement of pulse wave signal would be an asset for improving patient throughput and environmental impact.

To demonstrate its high functionality and fidelity for PWV measurements, we fixed our flexible pressure sensor to an adult human wrist, above the radial artery, as usually done in arterial tonometry (Figure 5). Figure 5a shows a real-time record over several pulse periods, together with a zoomed view on a pulse having the characteristic peaks typically measured at the radial artery. The location of the pulse wave foot—that is commonly used as a time reference for PWV measurements—is also indicated. Additionally, pulse wave velocity measurements are successfully performed using the same recording setup as above. As illustrated in Figure 5b, the pressure sensor is first attached above the carotid artery of an adult human, and the arterial pulse wave is recorded. Furthermore, the ECG is simultaneously recorded, being used for time reference. The pressure sensor is then placed above the femoral artery and the pulse wave and ECG are both again recorded. We then calculate the PWV to be 7.5 via: (i) the distance between the neck and the groin, according to clinical practice, and (ii) the time delay between the feet of the carotid and femoral pulse signals (Figure 5b), in which this obtained result is typical for a healthy subject.

Our single-use sensors are intended to be placed on human skin for typically several tens of minutes in a relatively dry environment for cardiovascular monitoring. However, it is important to verify that the device can withstand a short period of exposure to sweat in case of sweaty patient. As shown in Figure S8 (Supporting Information), the wrist pulse wave is successfully measured in all sweating conditions (Figure S8a–d, Supporting Information), even when the skin is entirely covered with artificial sweat (Artificial Eccrine Perspiration 1700-0020, Pickering). Moreover, the PHB/PHV top and bottom substrates offer an efficient protection against the corrosion of the metallization layers. This is illustrated in Figure S8e (Supporting Information), where a droplet of artificial sweat covers all the measurement area on top of the sensor. The sensor output is recorded for several tens of minutes, and the measured capacitance stays stable over time with less than 1% standard deviation.

In summary, we have described the design, fabrication, and characterization of a highly sensitive flexible pressure sensor entirely made of biocompatible and biodegradable materials. Our device’s high sensitivity in the low pressure regime (0.76 ± 0.14 kPa⁻¹ at p < 2 kPa and 0.11 ± 0.07 kPa⁻¹ at 2 < p < 10 kPa) in combination with its fast response time in the millisecond range makes it a highly promising sensor for point-of-care measurement of arterial stiffness and PWV.
range, is unprecedented when compared to recent reports on biodegradable pressure sensors. The pressure sensor performs stably after thousands of cycles. We also demonstrate a sensor array of $4 \times 5$ elements that allows the detection and localization of very light objects such as a grain of salt. An in vitro biodegradation study of PGS shows that this elastomer has a small hysteresis and little viscoelasticity behavior, with no significant changes even after seven weeks of incubation in a PBS buffer solution. These characteristics allow our pressure sensor to be useful for continuous cardiovascular monitoring, as illustrated by the acquisition of blood pulse wave signal at the human radial, carotid, and femoral arteries. The sensor is successfully employed to assess the pulse wave velocity, the gold standard for measuring subject's aortic arterial stiffness and therefore diagnosing hypertension.\(^\text{[7,8]}\) This sensor represents the first step toward realizing more complex biodegradable sensors that could potentially be used inside the body for biomedical applications such as pressure-assisted wound healing\(^\text{[13]}\) pressure-assisted hole drilling in the context of deep brain stimulation electrode implantation,\(^\text{[34]}\) intracranial pressure monitoring after traumatic brain injury\(^\text{[15]}\) or monitoring heart tissue pulsatile movements with sensor arrays combined with cardiac patches for the treatment of myocardial infarctions.\(^\text{[36,37]}\) Developing electrodes made of biodegradable metals with appropriate degradation rates and tailoring the packaging of these structures would permit preprogramming device lifetimes by temporally mediating exposure of critical device components, e.g., the metallization layers, to corrosive environments.

We envision that this work will contribute to fully biodegradable sensors for biomedical applications inside the body, with high pressure and strain sensitivity, intrinsic stretchability, and capable of distinguishing between pressure, strain, and bending.

**Experimental Section**

**Sensor Fabrication:** PGS was synthesized based on previously published methods,\(^\text{[20]}\) where an equimolar mixture of glycerol and sebacic acid was reacted at 120 °C under nitrogen for 24 h, resulting in a viscous uncross-linked PGS prepolymer. This prepolymer was further polymerized in oven at 130 °C in vacuum for 24 h. Afterward, the highly viscous prepolymer was cured at 130 °C for 24 h between a microstructured PDMS mold and a bare silicon wafer, both treated with a nonadhesive layer evaporated in vacuum (trichlorosilane, Gelest, USA). The PDMS mold (Sylgard 184 Silicone Elastomer, ratio 5:1) contains 2D arrays of square pyramids that are formed from arrays of pyramidal recesses etched into the face of a (100)-cut Si-wafer mold, as described in ref.\(^\text{[11]}\). After being cured at 130 °C in vacuum for 15 h, the ≈150 µm thick PGS film was peeled off and laminated with the bottom and top electrodes. The electrodes were fabricated by casting a thin polyvinyl alcohol (PVA) adhesive layer (40-88, Fluka Analytical, USA) on top of a 25 µm thick PHB/PHV film (8%, Goodfellow, USA), and evaporating iron (2 nm thick adhesive layer) and magnesium (100 µm thick electrode) after having exposed the substrate surface to oxygen plasma. The sensor was assembled by laminating the bottom electrode, intermediate PGS dielectric layer, and top electrode in vacuum. The PHB/PHV top and bottom electrodes were sealed previous to in vitro degradation study using a nonsolvent assisted thermal bonding process.\(^\text{[16]}\) For bonding, the sensor was placed in a custom-built mold made of PDMS (to equalize the applied pressure) and 50 µm thick Kapton polyimide films (to prevent sticking, Katco, UK) and sealed in a hydraulic press (Carver, USA; temperature: 155 °C, duration: 10 min, applied pressure: 1 MPa).

**Pressure Response Measurement Setup:** The measurement setup consisted in a motorized vertical stage used in combination with a force gauge, while the capacitance of each sensor was measured with an LCR meter.

In *In Vitro Study Cylinder and Stripe Samples:* A PGS film was polymerized and cut with laser (Versa Laser, USA), in order to produce PGS cylinder samples (diameter 7 mm, height 2.4 mm) and PGS stripe samples (width 4.4 mm, length 5 mm, thickness 2.4 mm).

**Mechanical Tests:** All tensile, compression, and viscoelastic mechanical tests were performed with an Instron 5565 Mechanical tester, used in compression and tension modes. Measurements were performed in controlled temperature and humidity atmosphere at $23 \pm 1$ °C and $50 \pm 10\%$ relative humidity. For tensile tests the strips were attached between two mechanical grips, while for compression tests the cylinders were compressed between parallel platforms using a lubricant between the sample and top/bottom plates to ensure proper mechanical deformation of the samples. For all experiments, the strain rate was 1 mm/mm min\(^{-1}\).

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**Supporting Information**

Supporting Information is available from the Wiley Online Library or from the author. A color version of Figure 1 to Figure 5 is also provided in Supporting Information.