Development of Piezoelectric Oscillator Sensor for In-Vivo Monitoring of Capsule Formation around Soft Tissue Implants

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ABSTRACT

Two types of piezoelectric wafer active sensor (PWAS) oscillators, Colpitts-type PWAS oscillator and series-type PWAS oscillator, designed for in-vivo monitoring of capsule formation around soft tissue implants have been presented. Both of the oscillators were explored analytically and experimentally. Colpitts-type PWAS oscillator uses the inductive property of the PWAS in its resonant frequency range and operates at the first resonant frequency of the PWAS. However, it is too sensitive to the surrounding damping. Therefore, it may not be an appropriate candidate for in-vivo application. For the series-type PWAS oscillator, some preliminary experiments showed that this type of oscillator can tell the difference in viscosity/damping conditions of different media. More work, such as calibration of output of the oscillator, needs to be done before using it in in-vivo monitoring of capsule formation.

Keyword: piezoelectric wafer active sensor, bio-PWAS, PWAS oscillator, implant, in vivo, capsule formation

1. INTRODUCTION

The cellular response to the placement of a foreign substance, particularly silicone, into the soft tissues has been fairly well characterized histologically [1][2]. The eventual replacement of a cellular phenomenon with fibroblast infiltration around the implant, followed by compact collagen deposition (the capsule) has been clearly documented. While some studies exist that have measured capsule mechanical properties, they are currently limited to static measurements of elasticity, compliance, and capsular pressure [3]. The development of long-term in-vivo measurement of dynamic mechanical properties of soft tissues will help improve the understanding of the biomechanical origin and process of capsular contracture. In addition, it could have tremendous application in early detection of capsular contraction, which can lead to poor clinical outcomes, around an implant placed during reconstructive or cosmetic surgery. Piezoelectric sensors have been developed elsewhere for a wide range of biological studies to determine cell growth and spreading on surfaces, to apply mechanical agitation locally to stimulate tissue growth, to detect minute concentrations of analytes in fluids, and to measure static mechanical stresses of tissue.

Previously [4],[5] we set forth to perform such dynamic measurements using piezoelectric wafer active sensors adapted for use as an implanted bio-sensor (Bio-PWAS) and the electromechanical impedance spectroscopy technique. Results indicate that only certain modes (first radial mode and thickness mode) in PWAS E/M impedance spectrum correlate with the state of the implantation, and that viscoelasticity of the tissue surrounding the implant changes in the different states of the implantation.

Therefore, it will be much simpler if it is possible to make bio-PWAS focus on just one resonance frequency and track how its value changes with various physical parameters in the different implantation states. A PWAS oscillator may meet this requirement. The resonant frequency of the PWAS oscillator depends on the effective mass

and stiffness of the PWAS, as well as its boundary conditions, soft tissue viscoelasticity, and soft tissue adhesion. If the mass changes due to surface adsorption and deposition, or the viscoelasticity of the surrounding tissue changes due to the evolution of implantation states, the resonant frequency responds by shifting. In this paper, two types of PWAS oscillators, Colpitts-type PWAS oscillator and series-type oscillator were designed and analyzed for in-vivo monitoring of capsule formation around soft tissue implants. Some preliminary experiments were also conducted to evaluate the performance of the PWAS oscillators.

2. PREVIOUS WORK—BIO-PWAS E/M IMPEDANCE APPROACH

2.1. PWAS E/M Impedance Theory

PWAS strain under an applied electric field. When driven under an alternating field, the PWAS oscillate over a spectrum of frequencies. At certain frequencies, the PWAS resonate and have a larger displacement. Since the structure of the piezoelectric material can be controlled during manufacturing, they can be made to possess characteristic motions (resonances) at specific frequencies. Figure 1 shows a diagram of the principal modes of vibration of a circular PWAS (thickness and radial). The radial vibrations occur over a range of lower frequencies ranging up from 100 kHz, whereas the thickness vibration occurs at much higher frequencies.

Figure 1 Principal modes of vibration of a circular piezoelectric wafer under oscillatory voltage excitation.

Giurgiutiu and Zagrai [6] have shown that the electrical impedance measured at the PWAS terminals depends both on the PWAS dynamics and on the impedance of the external medium. For circular PWAS resonators embedded in a medium with a given mechanical impedance, $Z_e(\omega) = \left\{ \left[k_e(\omega) - \omega^2 m(\omega) \right] + i\omega c(\omega) \right\} / i\omega = Z_{er}(\omega) + iZ_{el}(\omega)$, the electrical impedance measured at the PWAS terminals for radial mode vibrations is given by [7]:

$$Z(\omega) = \left\{ i\omega C(1 - k_p^2) \cdot \left[1 + \frac{k_p^2}{1 - k_p^2} \frac{(1 + \nu_a)J_1(\varphi_a)}{\varphi_a J_0(\varphi_a) - (1 - \nu_a)J_1(\varphi_a) - \chi(\omega)(1 + \nu_a)J_1(\varphi_a)} \right] \right\}^{-1} \quad (1)$$

where J_0 and J_1 are Bessel functions, k_p is the planar coupling factor, $\varphi_a = \omega r_a / c$, and $\chi(\omega) = Z_e(\omega) / Z_{PWAS}$. Equation (1) can satisfactorily predict the multi-resonance impedance spectrum for multi-resonance radial vibrations and various impedance functions of the external medium over a wide frequency range. A similar expression can be derived for the thickness mode vibrations.

2.2. Experimental Setup and Results

2.2.1. Experimental Setup

The materials used during these experiments included: (a) the bio-PWAS. It is a 7-mm diameter, 0.2-mm thick piezoelectric wafers with Nickel surface electrodes and connecting wires from APC International Ltd. The piezoelectric material prepared under manufacturer's specification APC-850 is Lead Zirconium Titanate (PZT). Prior to insertion in the laboratory animals, the bio-PWAS were sterilized in an autoclave using established procedure for sterilizing surgical instruments; (b) the laboratory animals. Twenty-six Sprague-Dawley lab rats weighing 200-300g were implanted with bio-PWAS dorsal midline near the cranium. For stability, the sensors were inserted and sewn into a slit in the latissimus dorsi muscle using Vicryl (absorbable) sutures (Figure 2a); (c) the measuring equipment. HP4194A impedance analyzer was used to measure the real and imaginary parts of the PWAS electrical impedance over a wide frequency band (Figure 2b). The frequency band of primary interest here is

the 100 ~ 900 kHz range, which covers the first and second resonance radial in-plane vibrations.

Figure 2 Experimental materials: (a) X-Ray of bio-PWAS implanted in rat #05; (b) HP4194A impedance analyzer

The time intervals at which the electromechanical impedance measurements were performed varied according to the processes being observed. At the beginning, when rapid changes were expected, the readings were taken relatively often (e.g., two readings at 30 min interval). As the observed processes became slower, the readings were also taken less often (e.g., only daily, and later at two-three day intervals).

2.2.2. Experimental Results

Figure 3 Evolution of the electromechanical impedance spectrum of bio-PWAS #BI05 immediately after implantation and a couple of days later [4]

Figure 3 shows the evolution of the electromechanical impedance spectrum followed immediately after implantation and for an additional couple of days. It was observed that the bio-PWAS impedance changes dramatically due to implantation (“Free” vs. “InRat”). The resonance peaks strongly decrease, the anti-resonance valleys strongly increase and the first in-plane mode frequencies shifted. Fast changes are also observed in the first hour after implantation, but the rate of change is not as strong as immediately after implantation. As time progressed, the rate of change decreased. By Day 2, the rate of change became much slower.

Figure 4 shows the evolution of the real-part impedance amplitude of the first radial mode vs. days from 4 bio-PWAS. The initial reading is of the sensor real-part impedance amplitude immediately following implantation,

which is taken as a baseline at 100%. The error bars represent the total variability in readings of 4 sensors, and analysis of variance indicates statistical differences among the mean amplitude values to a confidence of $P < 0.001$.

Figure 4 Bio-PWAS vibration amplitude as percentage of initial for the duration of the experiment. The double asterisk indicates a P value less than 0.005, whereas a single asterisk indicates a P value less than 0.05 compared with the values at 8 weeks. The error bars indicate the total variation in the data [5]

The recordings obtained from the PWAS directly reflected many of the findings observed morphologically [5]. At the time of PWAS implantation, an initial reading of radial amplitude was obtained. Two weeks later, as edema and cell inflammation occur, the amplitude is significantly dampened by approximately 50%, and this continues for the first month. The decrease in amplitude actually reflects an increase in surrounding tissue viscosity caused by the edema and cell infiltration. The dampening effect significantly increased during the period of early collagen formation out to 8 weeks, at which time the amplitude decreased to approximately 35% of the initial value. One may surmise that early collagen production around the sensor further increases viscosity of the tissue surrounding it, thereby impeding its radial motion. What was interesting was that at 12 and 16 weeks, the dampening lessened, and the radial motion amplitude of the sensor returned to approximately 45% of the initial reading. One possible explanation is that as the collagen bundles surrounding the implant mature—and the number of inter- and intra-molecular bonds increases — edema within the collagen bundles decreases. In this fashion, there is less impedance or inertial dampening (i.e., viscosity) to the vibratory motion of the sensor. Thus, one can envision the sensor more freely vibrating within the collagen envelope.

Figure 5 reveals the evolution of the real-part impedance spectrum for bio-PWAS implanted over a 20 week period. The animals were administered Celebrex – a non-steroidal anti-inflammatory drug (NSAID) as comparison to previous unaltered immune response recordings. Celebrex is unique because it selectively affects the COX-II enzyme as opposed to other anti-inflammatory medications that inhibit both the COX-I and COX-II enzymes. The COX-I enzyme is involved with the production of certain chemical messengers which cause inflammation and swelling.

Figure 5 Bio-PWAS vibration amplitude as percentage of initial for rats with Celebrex diet

In both figures 4 and 5, bio-PWAS respond very similarly during the first two weeks of the initial inflammation phase of wound healing – damping and frequency shift are on the same magnitude. At longer time periods, the differences between the plots in figures 4 and 5 stand out. In figure 4 (regular diet) bio-PWAS resonance was damped below 50% for readings taken after the first two weeks while readings taken at the 8, 16, and 20 week intervals (Celebrex diet) show resonances similar to the implanted readings without significant damping and frequency shift. While errors in the readings are significantly higher for resonant damping than the frequency response, they both show global trends that positively correlate to expectation. Specifically, bio-PWAS damping and frequency shift are expected to be minimized due to the presence of a selective anti-inflammatory medication because of its suppressive effects on the rat's immune response.

Qualitatively, the capsules that were formed in the absence of any enzyme suppressants were much more tightly adhered to the sensors and lead wires than capsules formed in the rats that were fed Celebrex. The soft tissue from the regular diet rats was also very difficult to remove from the lead wires upon dissection. Contrastingly, the soft tissue surrounding the rats fed Celebrex, once dissected, was slippery and easy to peel away from the lead wire insulation. A detailed report of the physio-chemical mechanisms affected by anti-inflammatory medications will not be presented here – rather the medications illustrate the sensitivity of bio-PWAS to soft tissue viscoelastic properties and cell adhesion characteristics between contrasting biological environments.

3. CONCEPT FOR PWAS RESONATOR AND PRELIMINARY RESULTS

3.1. Concepts for PWAS Oscillator

As it is shown in the previous section, the first radial mode of PWAS E/M impedance was of primary interest and was used to correlate the state of the implantation using E/M impedance approach for in-vivo monitoring of capsule formation. In addition, the viscoelasticity of the tissue surrounding the implant changes for different states of implantation. Therefore, it will be much simpler to focus on just one resonant frequency and track how its value changes with various physical parameters in different implantation states.

A PWAS oscillator may meet this need. The resonant frequency of the PWAS oscillator depends on the effective mass and stiffness of the PWAS and its surrounding conditions. If the mass changes due to surface adsorption and deposition, or the viscoelasticity of the surrounding tissue changes due to the evolution of implantation states, the resonant frequency also changes

Generally, basic oscillation circuits can be grouped into three categories: use of positive feedback; use of negative resistance element; use of delay in transfer time or phase [8]. Among them, the positive feedback oscillation circuit is widely used. Figure 6 shows the operating principal of positive feedback oscillator. For oscillation to occur, the Barkhausen criteria must be met: (1) the loop gain must be greater than one (2) the phase shift around the loop must be $n \times 360$ [8]. In the following section, two types of PWAS oscillators, Colpitts-type PWAS oscillator and series-type oscillator, designed for in-vivo monitoring of capsule formation around soft tissue, will be presented.

Figure 6 Principle of oscillation [8].

3.2. Colpitts-type PWAS Oscillator

3.2.1. Principle of Colpitts-type PWAS Oscillator

The performance of PWAS is most often analyzed using the simple electrical equivalent circuit of Figure 7 [9]. In this circuit, C_0 is the electrical capacitance between the two electrodes of the PWAS, while L_1 , C_1 and R_1 are chosen

to have a resonant frequency and Q factor numerically equal to those of the electromechanical resonance of the PWAS. RLC parameters of PWAS equivalent circuit can be readily measured by HP4194A impedance analyzer. For a free PWAS disc of 7-mm diameter and 0.2mm in thickness: $R_I=12.3422 \Omega$, $L_I=401.68 \mu\text{H}$, $C_I=691.1128 \text{ pF}$, $C_0=1.91798 \text{ nF}$.

Figure 7 Equivalent circuit of a bio-PWAS [9]

Figure 8 shows the superposed impedance and phase characteristics measured between the terminals of a free PWAS. The dotted lines represent the direct impedance measurement by HP4194A impedance analyzer. The solid lines were plotted by using the PWAS equivalent circuit parameters (R , L , C_0 and C_1 , see Figure 7). The plots illustrate that:

- The PWAS becomes inductive in the frequency zone between the frequency F_r (resonant frequency), which provides the minimum impedance, and the frequency F_a (anti-resonant frequency), which provides the maximum impedance.
- The PWAS becomes capacitive in other frequency zones.
- Equivalent circuit can be used to approximate PWAS impedance spectrum

Figure 8 Free PWAS impedance and phase characteristics: (a) impedance magnitude; (b) impedance phase

Figure 9 Colpitts-type PWAS oscillator schematic

Colpitts-type oscillator is a positive feedback oscillator using LC network. Therefore, in the Colpitts-type PWAS oscillator, the inductor L is replaced by the PWAS itself, taking advantage of the fact that the PWAS becomes inductive between resonant and anti-resonant frequencies (Figure 9).

After Pspice circuit simulation, schematic of Figure 9 was finally used to construct the Colpitts-type PWAS oscillator. Oscillation frequency of this circuit is expressed approximately by Eq. (2)

$$f_{osc} = Fr \sqrt{1 + \frac{C_1}{C_0 + C_L}} \quad (2)$$

where, $C_L = C_{L1}C_{L2}/(C_{L1} + C_{L2})$. Inverter1 works as an inverter amplifier of the oscillation circuit. Inverter2 acts to shape the waveform and also acts as a buffer for the connection of a frequency counter. R_f is the feedback resistor providing negative feedback around the inverter, so the oscillation will start, when power is applied. C_{L1} and C_{L2} are load capacitors.

3.3. Colpitts-type PWAS Oscillator Experiment

Figure 10 shows the experimental setup for the testing of the Colpitts-type PWAS oscillator. It consists of a frequency counter for frequency counting, an oscilloscope for waveform display and the oscillation circuit together with a free PWAS under test. To store the waveform for future analysis, a laptop with GPIB interface was also used in the experiment.

Figure 10 PWAS oscillator experimental setup

When driving a free PWAS, the Colpitts-type PWAS oscillator outputs strong and stable square wave at the PWAS resonant frequency (316.75kHz) (Figure 11). However, the oscillation circuit failed to drive a PWAS coated with silicon thin layer. It may be due to the dramatic change of the PWAS electromechanical property after applying silicon coating.

Figure 11 Colpitts-type PWAS oscillator output waveform (316.75kHz) when driving a free PWAS

3.4. Series-type PWAS Oscillator

3.4.1. PWAS Response to a Square Wave Input

A simplified equivalent circuit for the PWAS is the series RLC network, as shown in Figure 12. The PWAS shunt terminal capacitance C_0 is ignored here for simplicity but without losing generality.

Figure 12 Series PWAS oscillator [9]

A current-sampling resistor R_L is added in series with the PWAS, and the PWAS is driven by a step input of voltage E_i . The relationship between the applied voltage and resulting PWAS current is given by the Laplace transform [9]:

$$G(s) = \frac{e_i(s)}{i(s)} = \frac{L_1 s^2 + R s + 1/C_1}{s} \quad (3)$$

where, $R = R_L + R_1$. For a voltage step input, $e_i(s) = 1/s$. Using the inverse Laplace transform, the transient solution for the output voltage across R_L is found below:

$$E_0(t) = i(t) R_L = \frac{R_L e^{-t/(2RL_1)} \sin \left[\sqrt{C_1/L_1 - 1/4R^2 L_1^2} t \right]}{\sqrt{C_1/L_1 - 1/4R^2 L_1^2}} \quad (4)$$

As indicated by the above equation, the current through the PWAS is a damped sine wave and synchronized by the rising edge of the step input. Figure 13b shows the PWAS response to a 1 volt step input (Figure 13a).

If the step input is reversed (i.e., dropped back to zero) every time the current sine wave goes to zero at 180° and 360° , the exponential decay term drops out, and the transient solution becomes the steady-state solution. Figure 14 shows the PWAS response to a 333kHz square wave input. The PWAS response converges to a steady-state sine wave with glitches caused by the transitions in square wave.

Therefore, by applying a square wave to the PWAS at its resonant frequency – using the simple circuit in Figure 12, a sine wave will be perceived at the PWAS output. If the sine wave of PWAS current is fed into an amplifier with enough gain so that the amplifier output saturates, and if it also makes a square wave out of the sine wave and if this square wave is used to drive the PWAS, as shown in Figure 15, then conditions for a periodically reversed step input are obtained and there is continuous oscillation in the PWAS [9].

Figure 13 PWAS response to 1 volt step input: (a) step input; (b) PWAS response

Figure 14 PWAS response to 333kHz square input: (a) square wave input; (b) PWAS response

Figure 15 PWAS response to square wave [9]

3.4.2. Improved Series-type PWAS Oscillator Experiment

Based on the principle of PWAS response to a square wave input presented in the previous section, an improved series-type PWAS oscillator was constructed. Figure 16 shows the schematic of the series-type PWAS oscillator used in the experiment. The circuit operates sequentially in three stages: (1) current-sampling stage. A small value load resistor R_L is connected in series with the PWAS. When the PWAS operates at resonance frequency, the current flow through the R_L (in terms of voltage) reaches its maximum value. The value of load resistor R_L should be carefully selected to be in the order of the PWAS series resistance (R_s). This ensures that the energy from PWAS will be dissipated fast enough when the oscillator operates in high frequency. (2) Amplifier stage: a simple non-inverting amplifier was used to amplify the output from PWAS to amplifier's saturation range. Note that the amplifier selected should have high enough bandwidth and slew rate to start the high frequency oscillation. (3) Voltage follower stage: this is used to limit current and change the output impedance for connection to PWAS and frequency counter.

Figure 16 Series-type PWAS oscillator schematic

By adjusting the gain of the amplifier and load resistor value R_L , the oscillator will start to oscillate. Figure 17 shows a sample output waveform by series-type PWAS oscillator.

Figure 17 Series-type PWAS oscillator output waveform (~270kHz)

Table 1 Test of PWAS oscillator driving free PWAS coated with silicon in different media

Test Media	air	Water	AloeGe l	Petroleu m Jelly	auto trans. fluid	Baby Oil	Clay	Honey
Resonant freq. (kHz)	267.4	268.4	268.6	268.7	269.1	269.5	586.3	589.1

In the experiment, a free PWAS coated with silicon was tested in several different media with different viscosities (Table 1). With the increase of medium viscosity, the PWAS oscillator increases its resonant frequency indicating the change of its surrounding damping conditions.

As compared to Colpitts-type PWAS oscillator, the series-type PWAS oscillator is capable of resonating a heavily constrained/damped PWAS. Table 2 tabulates the resonant frequency of the series-type PWAS oscillator for driving a free PWAS and PWAS bonded to aluminum plate, as shown in (Figure 18). When constrained by the aluminum plate, the PWAS oscillator increases its resonant frequency to 602.7kHz.

Table 2 Test of PWAS oscillator driving free PWAS and a PWAS bonded to an aluminum plate

Status	free PWAS	mounted on a disc plate
Resonant freq. (kHz)	275.1	602.7

Figure 18 Free PWAS and a PWAS bonded to an Aluminum plate with adhesive

4. DISCUSSION AND CONCLUSIONS

Bio-PWAS and E/M impedance spectroscopy technique have been successfully used in in-vivo monitoring of

capsule formation around soft tissue implants. To reduce the data interpretation effort and simplify measurement instrumentation two types of PWAS oscillators: Colpitts-type PWAS oscillator and series-type PWAS oscillator were presented in this paper. Both of them were explored analytically and experimentally. Colpitts-type PWAS oscillator uses the inductive property of the PWAS in its resonant frequency range and operates at the first resonant frequency of a free PWAS. However, it is too sensitive to the surrounding damping. Therefore, it may not be an appropriate candidate for in-vivo application. For the series-type PWAS oscillator, some preliminary experiments showed that this type of oscillator can tell the difference in viscosity/damping conditions of different media. In addition, the oscillator is very robust to external constrain or damping. It is able to driving a PWAS mounted on an aluminum plate with adhesive. More work such as correlate the oscillator resonant frequency with the viscosity property of the different media and in-vitro tests of the oscillator need to be done before using it in in-vivo monitoring of capsule formation.

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REFERENCES

1. Smahel J, Hurwitz PJ, Hurwitz N, "Soft tissue response to textured silicone implants in an animal experiment", *Plast Reconstr Surg* 92, 474 (1993)
2. Picha GJ, Goldstein JA, Stohr E, "Natural-Y meme polyurethane versus smooth silicone: Analysis of the soft-tissue interaction from 3 days to 1 year in the rat animal model", *Plast Reconstr Surg* 85:903 (1990)
3. Giurgiutiu, V. (2002) "In-situ structural health monitoring, diagnostics, and prognostics system utilizing thin piezoelectric sensors", U.S. Patent Office Application Serial No. 10/072,644 of February 8, 2002, Attorney Docket No. 16139/09021 (under examination)
4. Giurgiutiu, V.; Friedman, H.; Bender, J.; Borg, T.; Yost, M. J.; Newcomb, W.; Black, A.; Bost, J.; Stewart, C. D. (2004) "Electromechanical Impedance Sensor for In-Vivo Monitoring the Body Reaction to Implants", *Journal of Investigative Surgery*, Vol. 17, No. 5, Sept-Oct. 2004, pp. 257-270
5. Bender, J. W.; Friedman, H. I.; Giurgiutiu, V.; Watson, C.; Fitzmaurice, M. (2005) "The Use of Biomedical Sensors to Monitor Capsule Formation around Soft Tissue Implants", *Annals of Plastic Surgery*, Vol. 56, No. 1, Jan. 2006, pp. 72-77
6. Giurgiutiu, V.; Zagari, A. (2000) "Characterization of Piezoelectric Wafer Active Sensors", *Journal of Intelligent Material Systems and Structures*, Technomic Pub., USA, Vol. 11, No. 12, December 2000, pp. 959-976
7. Giurgiutiu V.; Zagari, A. (2003) "Damage Detection in Thin Plates and Aerospace Structures with the Electro-Mechanical Impedance Method" submitted to *Structural Health Monitoring – an International Journal*, January 2003, log # SHM/01/2003
8. Murata Corp., "Ceramic Resonator Application Manual", *Catalog No. P17E-11*, 2004
9. Matthys, R. (1983), *Crystal Oscillator Circuits*, John Wiley and Sons, Inc, 1983