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Patient-Specific Self-Powered Metamaterial Implants for Detecting Bone Healing Progress

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There is an unmet need for developing a new class of smart medical implants with novel properties and advanced functionalities. Here, the concept of "self-aware implants" is proposed to enable the creation of a new generation of multifunctional metamaterial implantable devices capable of responding to their environment, empowering themselves, and self-monitoring their condition. These functionalities are achieved via integrating nano energy harvesting and mechanical metamaterial design paradigms. Various aspects of the proposed concept are highlighted by developing proof-of-concept interbody spinal fusion cage implants with self-sensing, self-powering, and mechanical tunability features. Bench-top testing is performed using synthetic biomimetic and human cadaver spine models to evaluate the electrical and mechanical performance of the developed patient-specific metamaterial implants. The results show that the self-aware cage implants can diagnose bone healing process using the voltage signals generated internally through their built-in contact-electrification mechanisms. The voltage and current generated by the implants under the axial compression forces of the spine models reach 9.2 V and 4.9 nA, respectively. The metamaterial implants can serve as triboelectric nanogenerators to empower low-power electronics. The capacity of the proposed technology to revolutionize the landscape of implantable devices and to achieve better surgical outcomes is further discussed.

1. Introduction

Smart implants with therapeutic benefits and diagnostic capabilities have shown a remarkable potential to revolutionize the healthcare system. For decades, smart implants have been deployed to measure and analyze various physical parameters from inside the body such as patients' pH and hormone levels, electrical activity, forces, strains, displacements, blood glucose, and temperature.[1] Real-time biofeedback provided by smart implants can play a key role in achieving better surgical outcomes. Data collected by smart implants can be used to refine the implant design and to improve surgical techniques and strategies. Despite the significant research carried out in the arena of smart implants, only a small fraction of them have become a part of our daily clinical practice. Two key issues constraining a wide application of the smart implant technologies are the device size for sensor integration and synthesis of scalable biomaterials for fabricating implantable devices.[1,2] Advanced wireless sensors offer new opportunities for designing smart implants. Unlike wired smart implants that are merely practical for preclinical research, wireless sensors foster development of implants that can take several measurements and communicate in real-time post-surgery.[2] Most of the current implantable telemetry systems utilize batteries or capacitors for operation. The use of energy storage devices in biomedical implants is associated with many issues such as short lifetime, size limitations, and chemical risks.[2] Passive or battery-free sensors are limited by the implantation depth

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and cannot record the data continuously unless they are powered by an external inductive/ultrasonic energy source.[2,3] Many of these passive implants use radio-frequency identification (RFID) technology to interrogate the sensor, which faces severe limitations inside the tissue.[3] Furthermore, signal corruption commonly occurs in the sensing circuits of the passive implants without sufficient filtering of the power supply voltage. Multiple circuit boards are required for sensing, power transfer, energy storage and wireless communications in active and passive smart implants.[2] The implants should be significantly modified in order to integrate these components into their very small area. Creating a new class of smart implants with intrinsic sensing and self-powering mechanisms could be the key to translating innovative implantable devices from lab to the operating rooms.

The other challenge ahead of smart implant technology is the lack of new biomaterials capable of achieving properties similar to human tissue.[4] Over the past five decades, researchers have been improving the composition of these metallic or polymeric materials to develop single-functional biocompatible implants mainly with better mechanical performance.[4] In order to mimic the extraordinary properties of the biological tissues, more attention has been recently paid to developing implants using novel classes of composites and nanomaterials.[4] The most recent innovation in the area of biomaterials for medical implants is the designer biomaterials concept, where rational geometrical design is used to build mechanical metamaterial systems with desired mechanical, physical, and biological properties.[4] Mechanical metamaterials are artificial structures, typically periodic, which are architecturally engineered to have specific properties that do not exist in a natural state.[5,6] Although incorporating architecture into material development is not a new concept, advanced fabrication techniques such as 3D printing have enabled the manufacturing of mechanical metamaterials with complicated designs. A recent study by Zadpoor[4] has revealed the remarkable potential of mechanical metamaterials to replace biological tissues via facilitating their regeneration. However, the entire concept of metamaterial for biomedical application is still in its infancy. So far, the only effort in the area of metamaterial implants has been a study on rational design of femoral stems with promising mechanical properties and biocompatibilities.[7] With the rapid development of smart materials and structures, more intelligent features are being incorporated into mechanical metamaterials.[8–10] Currently, there is urgent need for exploring new class of multifunctional metamaterial implants with novel properties and functionalities.

Here, we introduce the striking concept of "self-aware metamaterial implants" to create multifunctional implantable devices with built-in triboelectric nanogenerator (TENG) mechanisms. The self-aware implants can utilize their constituent components to achieve advanced functionalities. Without loss of generality, we deploy this concept to create a new generation of interbody fusion cage implants with self-sensing, self-powering and mechanical tunability functionalities for post-operative biomechanical evaluation of lumbar spinal fusion. We show how a self-aware metamaterial fusion cage can detect various levels of spinal fusion through continuous stability and load-sharing measurements directly at the intervertebral disc space level. These features could provide physicians the ability to assess the progress of fusion without the need for radiographic imaging. We perform experiential studies using synthetic and human cadaver spine models to verify the performance of the self-aware fusion cage system. We discuss the capacity of this scalable and cost-effective concept in changing the landscape of the patient-specific smart implantable technologies.

2. Results and Discussion

We demonstrate the first-of-its-kind mechanically tunable multifunctional metamaterial implant that can sense and harvest energy from body motions. The self-aware implant concept is inspired by our recent study on meta-tribomaterial sensor and nanogenerators.[10] A self-aware implant can be viewed as a composite meta-tribomaterial system with multi-stable/self-recovering snapping segments. We use different rationally-designed triboelectric auxetic microstructures to build a self-aware implant. The entire implant structure serves as an energy harvesting medium as well as an active sensing system. We adopted the term "self-awareness" from social psychology, where self-awareness is typically viewed as being aware of different aspects of the self-including behaviors and physical characteristics.[11–13] This is arguably the case for the proposed metamaterial systems because they are capable of collecting information about the operating environment directly using their intrinsic self-sensing and self-powering functionality. These metamaterial implants with a built-in TENG mechanism can offer unprecedented mechanical properties such as ultra-high strength-to-density ratios and high resilience. These properties are crucial for designing a mechanically robust implant.

We highlight the features and underlying mechanisms of the proposed technology by creating a proof-of-concept spinal fusion cage prototype. The reason behind this choice is that interbody fusion cages are widely used in treating conditions with lumbar spinal instability. Lumbar spinal fusion surgery is performed to treat spinal disorders such as degenerative conditions, deformity, trauma, and tumors. The number of lumbar spinal fusion surgeries performed each year in the United States exceeds 400 000.[14] The energy absorption functionality of the cages makes them relevant case studies for validating the self-aware implant concept. Current technology (i.e., radiography-based imaging techniques, wired load cells, active, and passive sensors attached to the spine fixation rods) is limited and does not have the specificity nor the sensitivity to determine spinal fusion.[2,15–17] In current commercialized devices, the progress of the fusion has limited means of confirmation. In most instances, follow-up radiographic observations including the use of plain film X-ray or dynamic flexion extension films may be ordered. It can be difficult to assess fusion on plain radiographs, and often computed tomography (CT) scans are employed. Even with advanced imaging, fusions still, at times, are difficult to fully confirm. Furthermore, common complications with spinal fusion procedures such as implant subsidence are difficult to evaluate using these techniques. A self-sensing interbody fusion cage can properly assess the progression of fusion by enabling measurement of the forces transmitted through the anterior column at the index level. Also, the implant subsidence could potentially be identified as a sharp decrease in the load applied to the device after endplate violation. **Figure 1** shows the vision for diagnosis of spinal fusion development directly at the intervertebral level using the proposed self-aware fusion cage. Spinal fixation devices are used to stabilize vertebrae movement. They allow bone graft materials to be packed inside interbody cages that fuse with the adjacent vertebra (Figure 1a). In this process, the interbody cage provides immediate stabilization of the functional spinal unit (FSU), transfers the loads between the fused vertebrae, promotes bone growth, and thereby improves fusion rates.[16] Figure 1b shows the composition of a self-aware interbody fusion cage. As seen, the implant is composed of rationally-designed conductive (electrode) and non-conductive (dielectric) triboelectric layers arranged in a periodic manner. The implant architecture is composed of parallel snapping curved segments with elastic snap-through instability mechanisms. These curved elements are designed to exhibit snap-through transition before and after deformation. The local support is provided by the clamped conditions of the snapping elements to prevent lateral displacement and bending at the ends of the semicircular-shaped slender elements. Figure 1c visualizes the physics mechanisms of the built-in contact-electrification in the implant. The spine force mechanically deforms (buckles) the semicircular-shaped segments of the implant. At a critical spine force, these segments snap from State I (stable) to State III (compacted). The implant microstructure is designed to induce a “self-recovering” snapping under spine loading. As a result, the fully compacted segments automatically return

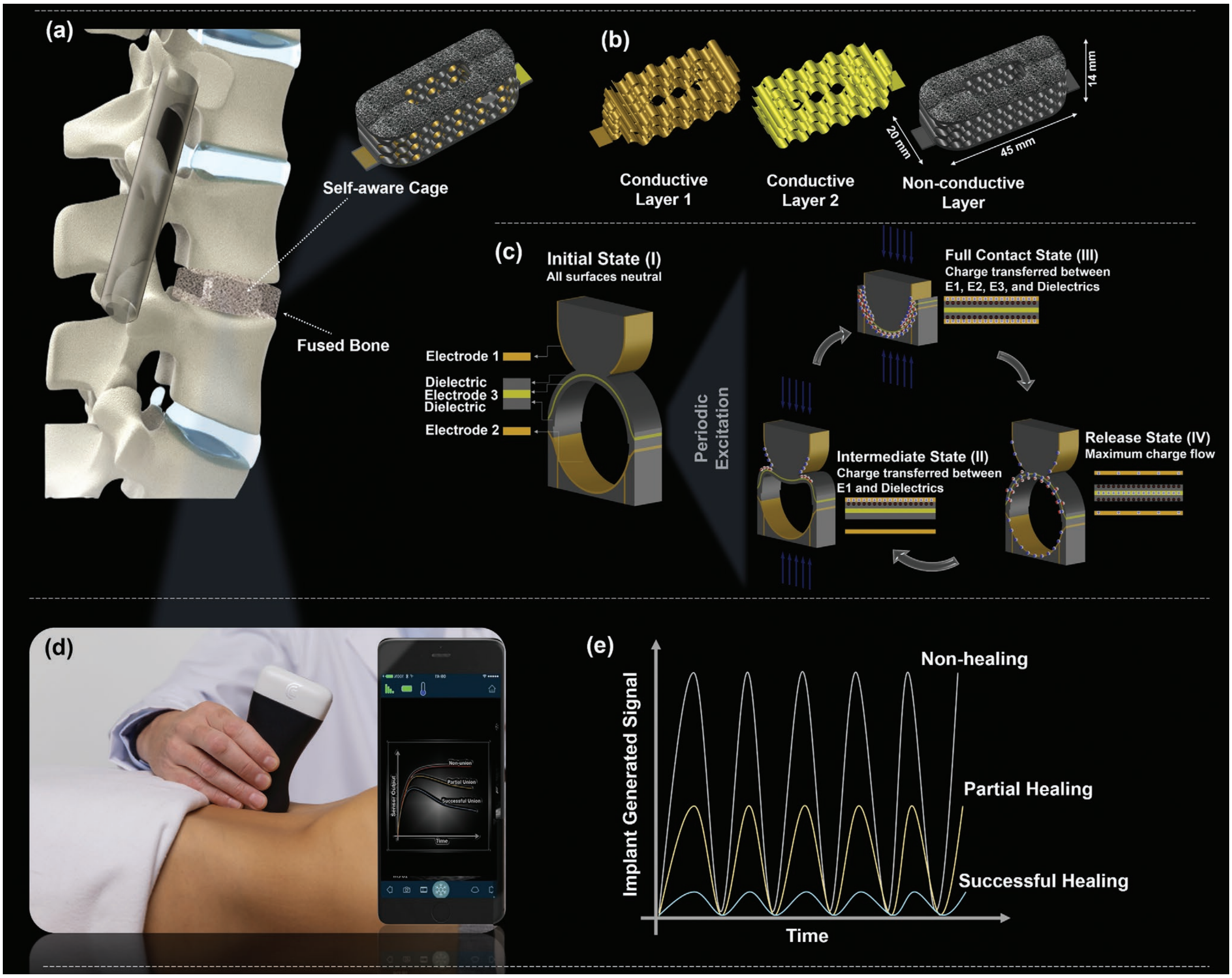

Figure 1. Vision of the proposed research showing a self-aware metamaterial implant that can be used for reliable determination of spinal fusion development post-surgery directly at the intervertebral level. a) A multifunctional nanogenerator interbody fusion cage with self-recovering, self-sensing and energy harvesting functionalities implanted during spinal fusion surgery. b) Composition of a self-aware cage implant. The implant generates electrical signals due to spine micro-motions using its built-in contact-electrification mechanism. The signal can be used for sensing and energy harvesting purposes. c) Physics mechanisms of the built-in contact-electrification in self-aware implants. d) The recorded data will be retrieved using an FDA-compliant portable ultrasound scanner. This figure shows a Clarius C3 HD3 ultrasound scanner. e) The sensor output signals represent various healing stages and can be correlated with the changes of FSU stiffness due to the healing process.

to their initial stable configuration after the load is removed. Under spine micro-motions, contact-electrification will occur between the conductive and non-conductive layers of the implant. This contact-electrification process will generate an electrical output. Spinal fusion rods and cages typically share the load applied to the spine post-surgery. During the initial stages of the healing process, the cage and rods carry the majority of the spine load, but eventually, the fusion hardware becomes obsolete once the arthrodesis occurs.[15,16] The changes in the loading conditions of the smart cage can be used for the long-term assessment of the healing process. The voltage signal generated by the cage is proportional to the forces applied to its structure. Higher loading amplitudes create larger deformations. Consequently, the number of layers engaged in the contact–separation process increases leading to a larger voltage. The proposed diagnostic mechanism is based on a "relative healing" diagnostic approach. The term relative healing implies that the signal generated during the healing process should be compared with the previous stage and a "reference baseline". During the spinal fusion surgery, the surgeon will pack the bone graft inside the purposely designed large opening/cavity in the middle of the cage (see Figure 1a). The reference baseline voltage will be the initial voltage generated by the cage filled with the graft. This is the first stage of the fusion representing an "unhealed" fusion stage. As the bone starts forming inside and around the cage, it will start interfering with more unit cells, making the cage stiffer and reducing the stress on the cage and the corresponding voltage. As bone heals, the load will be transferred to the fused vertebrae and the amplitude of forces exerted to the cage will continuously decrease. As a result, the voltage generated by the cage will decline over the course of fusion. The changes in the loading conditions (mechanical usage) of the cage would shift the voltage from the reference baseline during the course of the fusion. Upon osseous union, the spine load will be carried mostly by the fused bone. In this stage, the deformation of the cage will be at its minimum (close to zero) and will not be enough to generate any voltage. These changes in the signal patterns during the healing process can be coupled with available miniaturized wireless data logging technologies (e.g., Ref. [2]) to record its mechanical usage over time. As seen in Figure 1d, the collected data by data loggers can be wirelessly retrieved using an FDA-compliant portable ultrasound scanning system, as shown in ref. [3]. The data could be correlated with the changes of FSU stiffness due to the healing process (Figure 1e).

However, one of the advantages of the proposed implantable technology is that the implants can be fabricated using a wide range of biocompatible (e.g., Au, Al, Ti, ethyl cellulose (EC), polylactic acid (PLLA), polydimethlysiloxane (PDMS), etc.) and bioresorbable metallic or polymeric (Magnesium, poly(3-hydroxybutyric acid-*co*-3-hydroxyvaleric acid) (PHB/V), poly(caprolactone) (PCL), and poly(vinyl alcohol) (PVA), etc.) materials with triboelectric properties. The self-aware implants are structure-dominated, scale-independent multifunctional mechanical metamaterials. Thus, depending on the targeted application, their shape, size and stiffness can be readily tuned by changing the number and deformation sequence of auxetic cells, assembly of microstructures, and layers material. This could result in design of personalized and patient-specific implants (PSIs) facilitated by many of the existing additive manufacturing (AM) techniques. A PSI that exactly matches the patients' anatomy could potentially improve primary stability and increase the lifetime of the implants.[18] Furthermore, a self-aware cage implant serves as a bony modulus matched expandable cage because of the self-recovering mechanism integrated into its design. Compared to the commercially available expandable cages, the cage offers higher bone fusion area and ease of insertion, as well as a more efficient biomimetic design capturing native bone porosity for better bone growth because of its customizable auxetic structure. The porous, self-recovering and tunable structure for the cage or similar self-aware implants could effectively reduce the stiffness to "mitigate the stress shielding effect", to minimize cage subsidence and to obtain more comparative strength for the surrounding tissue.

Here, we fabricate proof-of-concept PSI fusion cage porotypes and test them using synthetic biomimetic and human cadaver spine models. Based on the arrangement of conductive and nonconductive parts, and also the geometry of the metamaterial, the dominated triboelectric mode is contact-separation. **Figure 2** shows the fabrication process of the self-aware metamaterial implants. Two porotypes with different dimensions were fabricated. The first sample was designed to fit within the synthetic spine disc space for preliminary studying of the implant performance (Figure 2e).

The second sample was fabricated according to the geometry of the spinal motion segments derived from the CT scans of the lumbar spine of a 55-year-old male (weight: 86.6 kg, height: 165.1 cm) (Figures 2a,e), while its elastic material properties were designed to be within the ranges reported for lumbar intervertebral discs.[19–23] The length, width, and height of the first sample were 45, 20, and 14 mm, respectively. These dimensions were, respectively, 32, 16, and 13 mm for the second cage implant designed for the human cadaver spine model. Surgeons are generally recommended to use fusion cages with maximal surface area to enable packing more bone graft.[24] Accordingly, we considered a fairly large cage to disc surface area ratio (≈0.6) for the samples. In clinical practice, a patient may even require wider cage because of circumstances found at the time of surgery.[24] The thickness of the conductive layers was ranged between 0.1 and 0.2 mm during the numerical simulations. The inside radius of the circular segments was set to 1.4 mm. In this study, we used Thermoplastic Polyurethane (TPU) and Polylactic Acid (PLA) with carbon black to fabricate the dielectric and conductive layers, respectively. We chose TPU and PLA because they are both biocompatible with the human body.[25,26] Also, they are, respectively, on the negative and positive sides of the triboelectric series,[27] which is an important factor for increasing the triboelectrification. The human lumbar spine has low-frequency vibrations normally within a range of 1–8 Hz.[28,29] We chose a relatively low frequency (0.25 and 0.5 Hz) to ensure the sensing capability even under quasi-static or very low-frequency condition, as well as persevering the spine models under the loading cycles. Also, the axial force on spine usually ranges from 200 N (in relaxed sitting or lying position) to 1000 N (during upright standing or sitting).[30] Furthermore, in tests using synthetic spines, a maximum non-destructive axial compression of 350 N is recommended.[31,32] Accordingly,

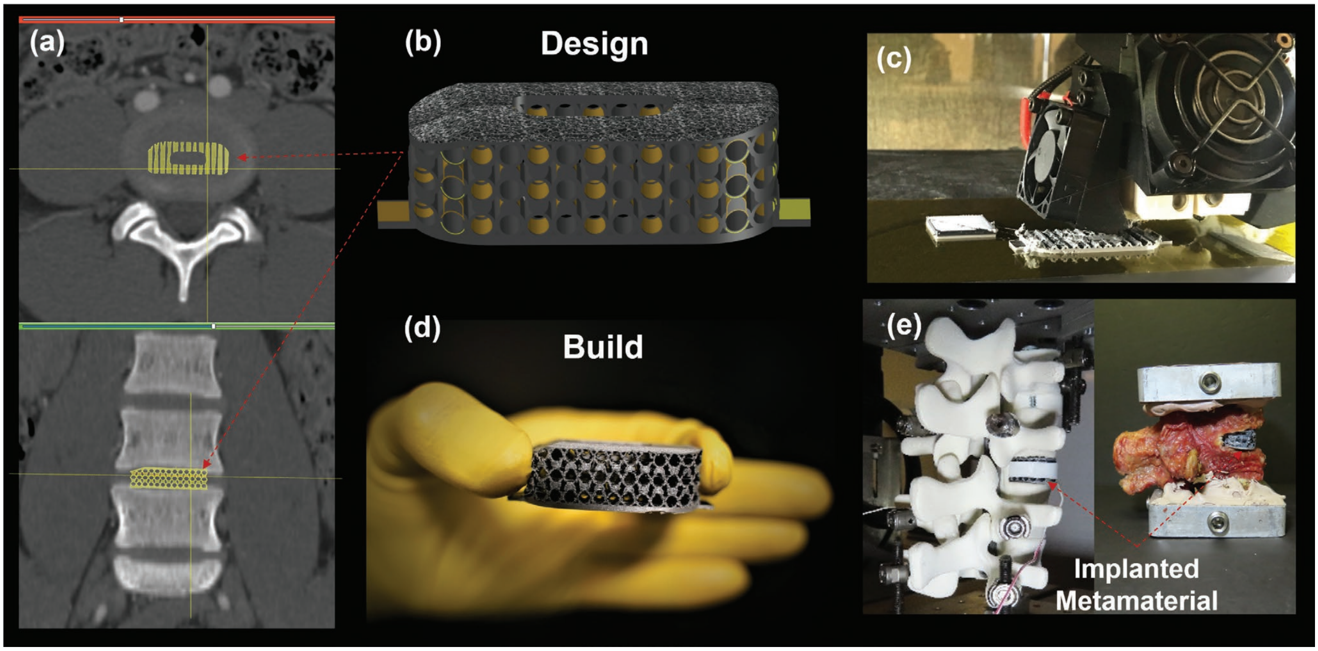

Figure 2. Fabrication process of the proposed self-aware metamaterial implants. a) CT scans showing the cadaver spine segments (Photo copyright, Allegheny General Hospital). The implantable self-aware interbody fusion cage is schematically shown on the radiographs. The PSI cage implants are designed based on the geometry of the spinal motion segments derived from the CT scans. b) The 3D model of the prototype interbody fusion system matching the patient's anatomy. b) 3D printing of the fusion cage. c) The fabricated patient-specific fusion cage. d) The self-aware fusion cage implanted inside synthetic and human cadaver spine models.

we chose 325 N which corresponded to a 3 mm displacement. The first set of experiments were carried out using a synthetic biomimetic lumbar spine model (Sawbones, WA, USA) at the L3-L4 vertebrae level. The first cage specimen was implanted on the posterior segment. As shown in Figure 2e, the synthetic spine model was securely attached to the top and bottom plates using special fixtures. Tests were performed under displacement control condition with displacements ranging from 0 to 3 mm. **Figure 3** shows the results of the experimental studies on the spine cage implanted inside the synthetic spine model at the initial stage of the healing process. As seen in Figures 3a,b, the self-aware cage is capable of generating 9.2 V and 4.9 nA under compressive loading. Low-power electronics can be empowered using the electrical energy generated by the nanogenerator cage implants. Hence, it is of utmost importance for the prototype to demonstrate its charging capability. Since the output signal of the sensor under the cyclic mechanical compression load has a periodic characteristic, it can be referred to as an AC signal. To that end, the main objective of energy harvesting applications is to charge some form of storage (i.e., a battery or a capacitor). With a simple full bridge rectifier circuit, the self-aware implant has the ability to charge the output capacitor with the behavior modeled in Figure 3c. As soon as the loading starts, the capacitors are charged at maximum speed. Gradually, the charging speed decreases until it is fully charged. As seen in Figure 3c, the saturation voltage is ≈8 V, which is about 1 V less than the maximum voltage shown in Figure 3a. The comparison of the stored charge in the capacitor over time, shown in Figure 3d, provides sufficient knowledge about the behavior of the sensor as a charging source. Figure 3e presents the voltage and charge stored in the capacitors after 30 s.

In addition, we performed bench-top testing using the synthetic spine model to evaluate the performance of the proposed smart cage system for detecting various fusion states. **Figure 4** illustrates the test setup and self-aware interbody fusion cage placed inside different rings. The encapsulating rings were 3D printed using PLA with gradually increasing stiffness (10–100% infill density) to simulate the spinal fusion process. This simulated osseous union phase using filler materials, as reported in a recent study by the authors,[2] was merely designed to characterize the patterns of the voltage generated by the cage due to the FSU stiffening emulated by increasing the stiffness of the encapsulating rings. In fact, exact simulation of the fusion process has not been done in vitro so far due to complicated biological mechanism involved. While the simulated fusion does not represent the exact mechanical behavior of the fused bone, it provides important information about the correlation between the dynamics of the implant signal and the bone healing. The number of loading cycles, amplitude and frequency were 50, 300 N, and 0.5 Hz, respectively. The fusion cage was first inserted inside the disc space without an encapsulating ring to investigate a non-healing state, where the entire spine load is carried by the implant. Then, different rings with increasing stiffness were placed around the spinal cage to simulate the healing progress. Fifty loading cycles were applied during each stage. Five spinal fusion states (FS) were considered as follows

- FS1: 10% infill
- FS2: 25% infill
- FS3: 50% infill
- FS4: 75% infill
- FS5: 100% infill

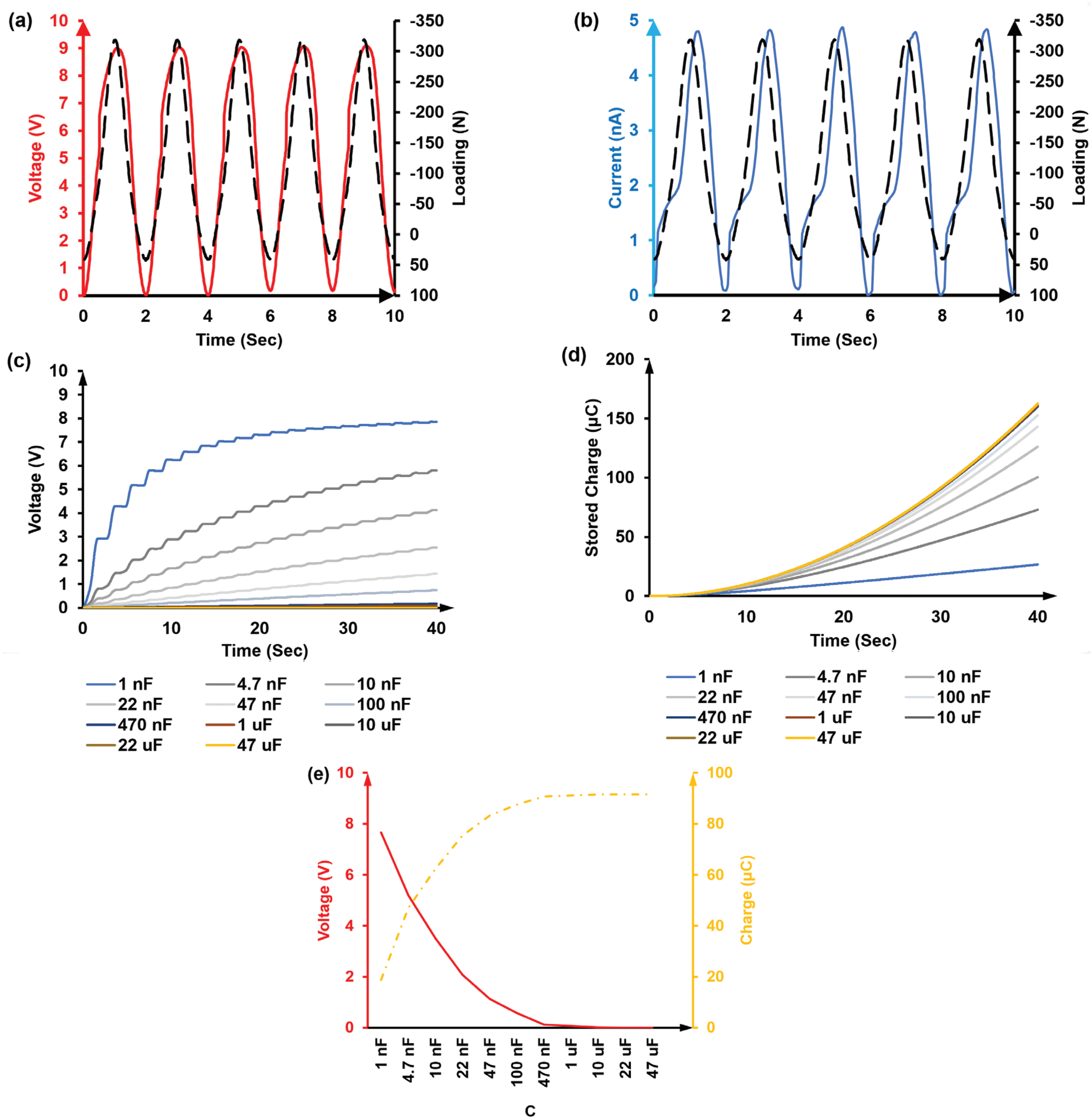

Figure 3. Synthetic spine model test results showing: a) Voltage (in red) generated by the self-aware interbody fusion cage. b) Current (in blue) generated by the self-aware interbody fusion cage, c) voltage-time for different capacitances. d) Stored charge-time for different capacitances. e) Voltage and charge stored in the load capacitor at 30 s.

The voltage values generated by the cage during various fusion states are shown in **Figure 5**. Video S1, Supporting Information shows a typical voltage signal generated by the cage implanted inside the synthetic spine model. During the non-healing state, maximum load is exerted on the fusion device. As seen in Figures 5a,d, the highest voltage is generated during the simulated non-healing state. Using rings with higher stiffness represents the healing progression. As the rings become stiffer, they carry larger portions of the load. This reduces the level of load-induced strains inside the cage resulting in generating lower voltage values, as shown in Figures 5a,b. As the spine healing process continues, the cage voltage decreases proportionally. In FS5, a 100% infill density disc was used to simulate a successful osseous union. In this case, almost the entire load is carried by the ring. While the deformation of the cage is not exactly zero at this stage, it is small enough not to generate any signals. This successful osseous union state corresponds to the lowest measured voltage. This observation

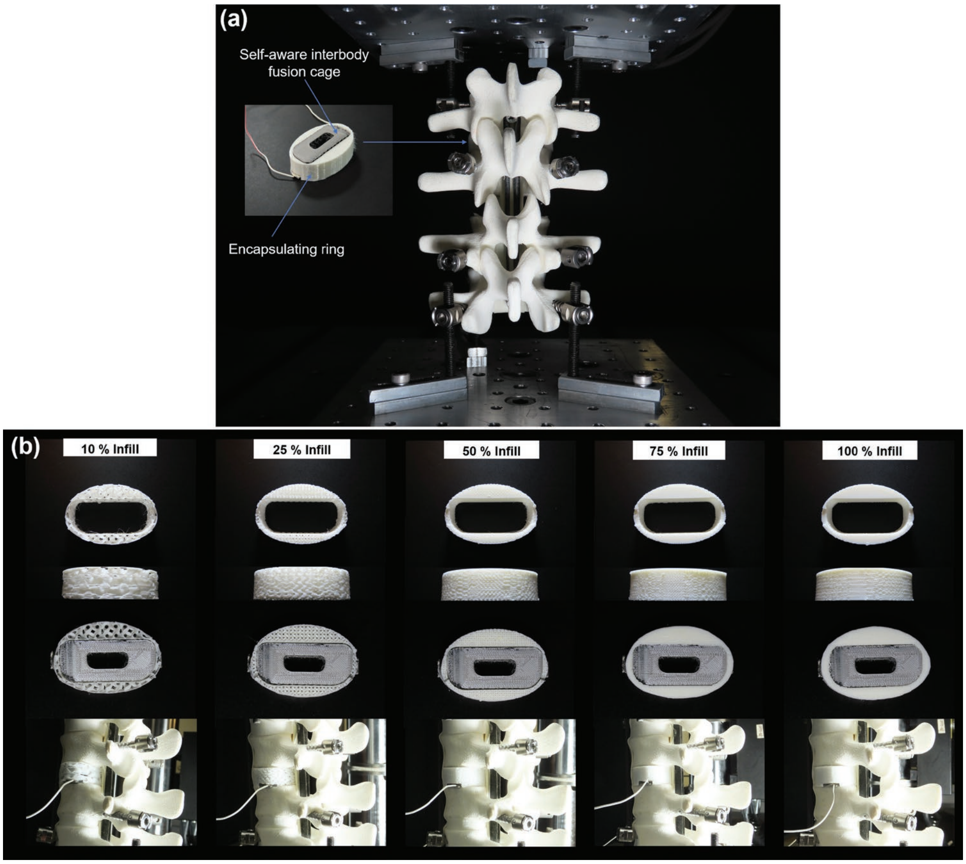

Figure 4. Spinal fusion monitoring process using the proposed self-aware fusion cage system. a) Test setup including synthetic biomimetic spine model with the fusion cage and encapsulating ring implanted at the L3-L4 vertebrae level. b) Simulated spinal fusion using the fusion cage encapsulated in rings with varying stiffness.

implies that load transfer gradually shifts from the fusion cage to the bony bridge within the fused segment.

In order to evaluate the electrical and mechanical performance of the proposed spine fusion cages, we further carried out fatigue tests using the synthetic spine model. For the fatigue study, the second porotype was subjected to 40 000 axial loading cycles at 0.5 Hz frequency with a 350 N axial compression force. The fatigue test results are presented in Supporting Information. The cage elastic modulus (E) decreased from 1.76 to 1.4 MPa after 40 000 loading cycles (Figure S2, Supporting Information). The generated voltage dropped with a high slope from 2.69 to 1.31 V during the initial 10 000 cycles (Figure S6, Supporting Information). The voltage remained close to 1 V over the rest of the fatigue test. The observed trend in voltage is the result of changes in both mechanical and electrical properties of the spinal fusion cage. Charge carrier density decreases over time in the proposed built-in TENG system. Decline of the electrical and mechanical performance under thousands of

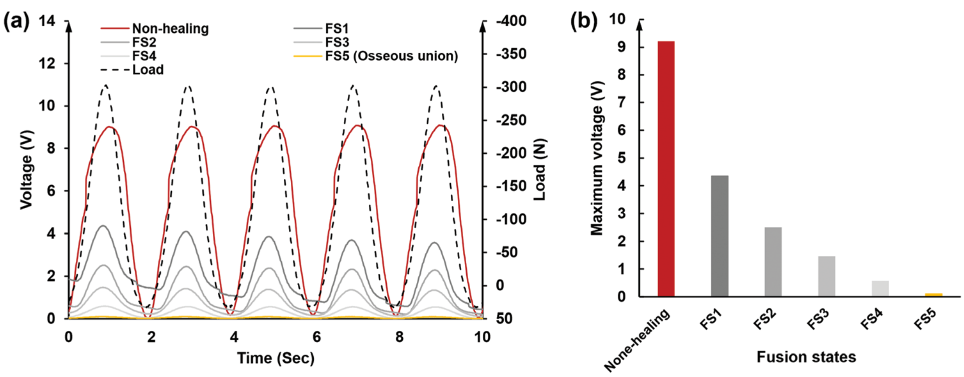

Figure 5. Self-aware fusion cage outputs corresponding to different fusion states for the synthetic spine model. a) Generated voltage corresponding to different fusion states subjected to the cyclic loading. b) Maximum generated voltage in each fusion state.

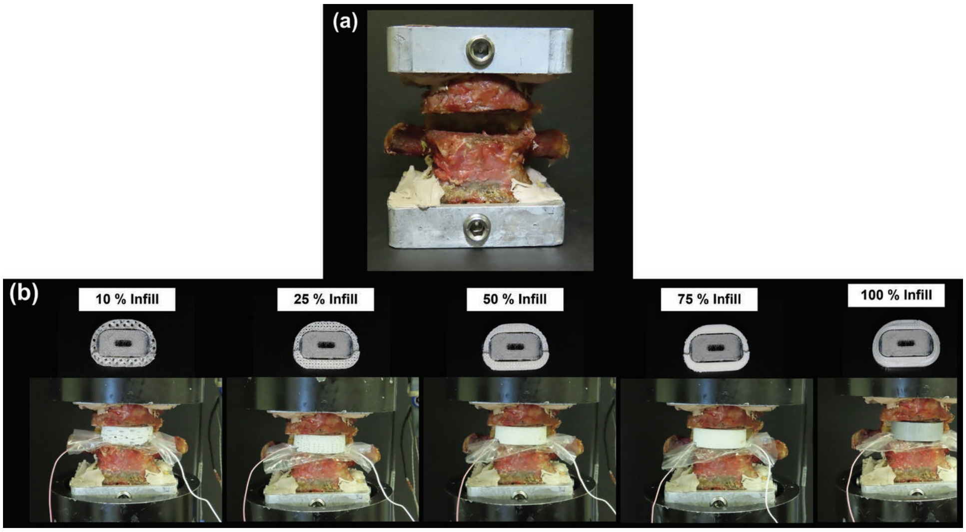

Figure 6. Spinal fusion monitoring process using the proposed self-aware fusion cage system implanted inside the human cadaver spine model. a) Test setup including the fusion cage and encapsulating ring implanted inside the L4–L5 cadaver spine segments. b) Simulated spinal fusion using the fusion cage encapsulated in rings with varying stiffness.

cycling loadings is expected and should be carefully studied to find calibration parameters for various classes of patient-specific implants. It should be noted that a desirable performance for a spine fixation device varies case by case. The target performance does not necessarily need to be the maximum electrical output or mechanical performance and heavily depends on the clinical requirements. However, synthetic spinal constructs have different stiffness properties compared to the animal or human vertebral models. This issue causes difficulties in the measurement of realistic bone strains.[33,34] Based on several biomechanical studies,[34,35] human cadaver studies have provided the best indication of bone strains during loading of the spine. Arguably, the cadaver models are essential to allow evaluation of strain levels expected during spinal fusion in patients. Therefore, we further study the performance of the proposed self-aware interbody fusion cage for the in vitro monitoring of spinal fusion in human cadaver models. To this aim, a fusion monitoring process similar to that considered for the synthetic spine was conducted using human cadaveric spinal segments. We used the fusion cage with stabilized voltage signal after the fatigue testing. The spinal segment used for testing was isolated from a 55 year old male donor with a DEXA T-score of –1.4, indicating osteopenia. To simulate the entire bone fusion process, a complete discectomy was performed at the L4-L5 index level with care taken to remove all soft tissue down to the endplate (**Figure 6**a). Then, 3D printed rings with different infill densities were used to fill the intervertebral disc space. Fifty axial compression loading cycles with an amplitude of 500 N at 0.25 Hz frequency were applied to the cadaver spine with implanted fusion cage at each stage (Video S2, Supporting Information). Figure 6b presents the test setup with different filler rings with 10–100% infill density. The measured voltage values for different healing states are shown in **Figure 7**. Stiffer rings representing a fusing bone reduced the level of load applied to the cage. In this case, the spinal cage sensor produced a lower voltage (Figure 7a). Decrease in voltage indicates the progress of the spinal healing process. Similar to the synthetic spine tests, the lowest voltage recorded was at FS5 during the cadaveric tests. FS5 denote a ring with 100% infill density and accordingly a successful osseous union.

However, the presented proof-of-concept prototypes demonstrate the first application of the self-aware metamaterial

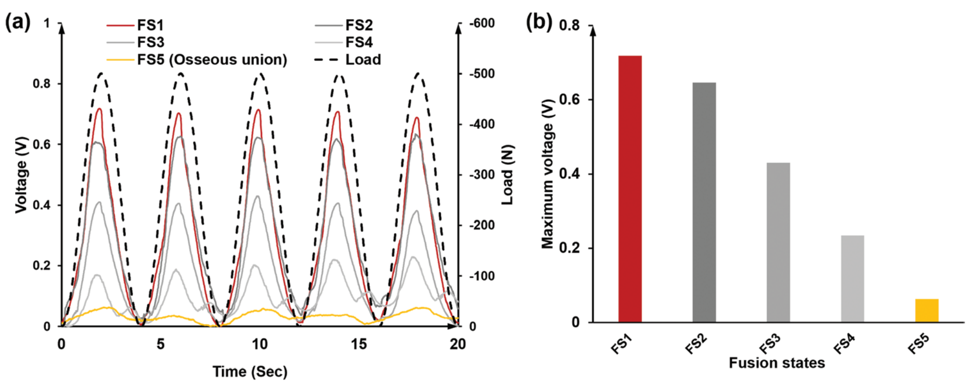

Figure 7. Self-aware fusion cage outputs corresponding to different fusion states for the human cadaver spine. a) Generated voltage corresponding to different fusion states subjected to the cyclic loading. b) Maximum generated voltage in each fusion state.

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implants for biomedical sensing, monitoring and energy harvesting. The mechanical and electrical performance of self-aware implants should be customized for each patient based on the clinical requirements and anatomical matching. The results reveal the capacity of the proposed concept in pushing the limits of medical implant technologies without using any external power source and bulky electronics. Since the implant itself could serve as a sensor and energy harvesting medium, little to no modification to existing implant designs would be required. The self-aware implants can continuously collect the data due to any mechanical stimuli. Wireless interrogation of the implant measured data is a challenging task. A viable solution is to couple the signal generated by the self-aware implants with ultra-low-power consumption (<100 nW) wireless data logging technologies (e.g., Refs. [2, 36–39]) to create fully self-powered systems. This can be done through a passive strategy where a range of spinal motions will be induced by asking the patients to acquire a predetermined number of sitting and standing postures during therapy sessions. The voltage response of the cage implant corresponding to each posture can be recorded and will be assessed at various stages of the healing process. A limitation of this approach is that it evaluates the fusion condition at a given moment and presents only a "snapshot at the time" where the measurements are taken. It is also feasible to design a semi-active strategy by coupling the data-loggers with the cage electrical signal to continuously record its mechanical usage over time. This way, the data-logger serves as a non-volatile storage memory that can potentially record all in vivo events and aggregate the short-term fluctuations. The signal patterns stored by the data-loggers in both passive and semi-active approaches can be retrieved using a telemetry interface. For instance, mm^3 sized sonomicrometry crystals can be fully integrated with the data-loggers and an ultrasonic encoder/driver on a single chip for wireless interrogation of the implant.[40–42]

Such a powerful experimental tool would enable design of the next-generation healing monitoring technologies for other treatments and therapeutics of fracture repair. A self-aware implant would naturally inherit the outstanding features of the TENGs, which have significantly high-volume power density (≈500kW m^{-2}).[43–45] This energy can be used to empower other miniaturized low-power consumption electronics in vivo. Furthermore, electrical stimulation (ES) has proved to be an effective method to enhance bone healing.[46] There are a number of FDA-approved invasive and noninvasive electrical stimulation devices currently being used for bone growth stimulation in a variety of orthopedic conditions.[46] These devices administer electrical current to the bone which commonly include direct current (DC), pulsed electromagnetic field (PEMF), capacitive coupling (CC), or inductive coupling (IC). In this area, using the electrical signal generated by a self-aware implant to accelerate bone healing and changing growth factors could open the doors for widespread application of smart implants in therapy for fracture healing.

Figure 8 presents a vision for creating 3D nano-, micro-, meso-, and macro-scale implants under the proposed concept. Orthopedic self-aware implants seem to be the most immediate application area. Topology analysis can be performed to create various types of orthopedic implants, for example, tibial tray and acetabular cup. Other medical fields can also benefit from this technology. For instance, stents are extensively used in cardiac surgeries. Despite their clinical efficacy, they may cause a

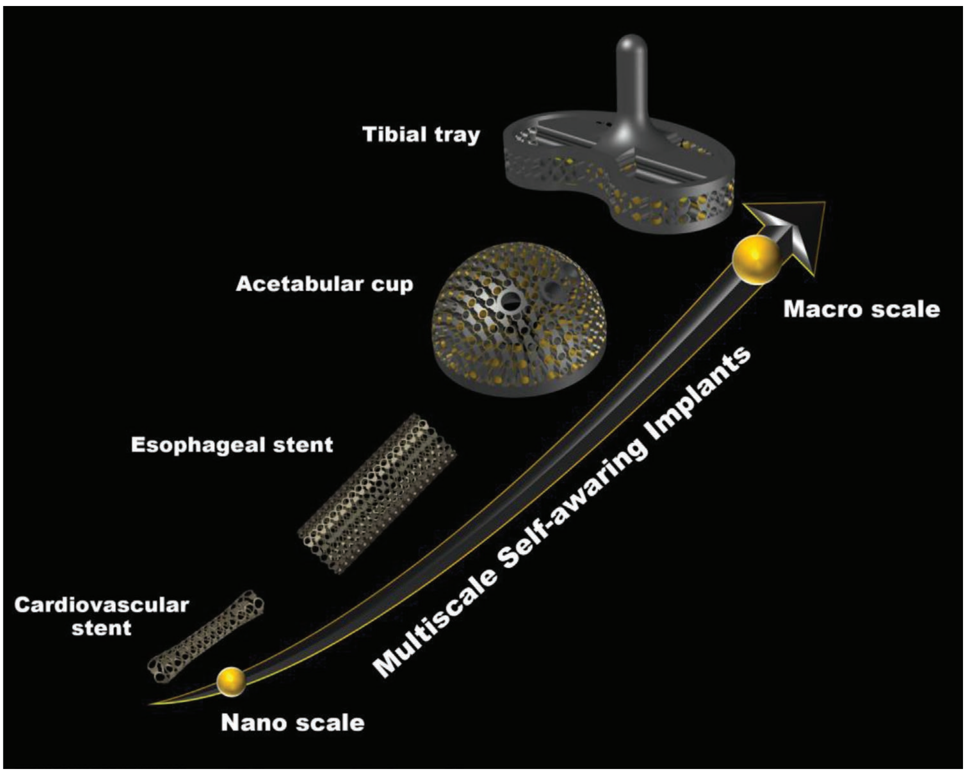

Figure 8. A vision for creating nano-, micro-, meso-, and macro-scale implants under the proposed concept.

complication called in-stent restenosis.[47] Currently, there are not any implantable system that can detect this complication at early stages. A biocompatible self-aware cardiac stent can be used to monitor any local hemodynamic changes due to in-stent restenosis. In a similar manner, a self-aware esophageal stent empowered by esophageal peristalsis can monitor the local esophagus wall radial compressive forces changes caused by stent migration and tumor overgrowth. However, rational design of such multifunctional smart implants requires targeting various physical property types. Accordingly, a multi-physics design approach should be adapted to mimic the complex properties of the biological tissues.[4]

3. Conclusion

In summary, we presented the novel concept of self-aware metamaterial implants. We leveraged advances in nanogenerators and the metamaterial to introduce new aspects of multi-functionality into the fabric of medical implants. We fabricated first-of-its-kind interbody fusion cage prototype and demonstrated the feasibility of the proposed approach for self-powered monitoring of bone healing without using any external power source and without any loss of data. The experimental studies performed on both synthetic spine and human cadaver spine models confirm the efficiency of the self-aware implants in assessing fusion process and harvesting energy from mechanical excitations. Under loading conditions similar to human lumbar spine, the fusion cage porotype can generate voltage and current values equal to 9.2 V and 4.9 nA, respectively. A series of fatigue tests using the synthetic spine model revealed that the cage elastic modulus drops from 1.76 to 1.4 MPa after 40 000 loading cycles. The generated voltage drops from 2.69 to around 1 V. The results imply the necessity to develop more robust fabrication and calibration methods for such patient-specific implants. The proposed concept could open avenue for the next stage of the revolution in smart implantable devices, where a new generation of scalable, cost-effective, multifunctional, and personalized implants could be widely used by clinicians to achieve better surgical outcomes. Our future research will focus on developing a series of mechanically and electrically-optimized self-aware metamaterial cage implants for in-vivo testing in large animal models.

4. Experimental Section

Fabrication of the Self-Aware Interbody Fusion Cages: In this study, TPU (E = 12 MPa, ν = 0.48) and PLA with carbon black (Young's modulus E = 3000 MPa, Poisson's ratio ν = 0.25) were, respectively, used to fabricate the dielectric and conductive layers of the fusion cages. PLA and TPU are on the negative and positive sides of the triboelectric series, respectively. This combination maximized the electrification between the layers. 3D models of the cages were first created using AutoCAD and SolidWorks based on the geometries of the synthetic and cadaver spines. Three different segments of the proposed implants were fabricated using the fused deposition modeling (FDM) method and a Raise3D Pro2 Dual Extruder 3D Printer. All layers of the interbody fusion cages (i.e., electrodes and dielectric layers) were printed simultaneously. After the printing process finished, the supports and extra printed parts were removed from implants. The implants were tested without any additional post-printing modifications.

An Instron 8874 universal testing machine was used to test the spine samples. The cadaveric specimen was mounted for testing using customized fixtures and a polyester resin and hardener (Bondo, 3M) to enable testing on a 6 degree-of-freedom spine tester (Bose Smart Series). The LabView software interfaced with an NI9220 module (1GΩ impedance) was used to record the generated voltage values. The current generated by the fusion cages was measured using SR570 amplifier (Stanford Research Systems).

Anatomical Materials: This study was a cadaveric investigation and did not involve human subjects. Therefore, institutional review board approval was not necessary for the research presented in this article. Allegheny General Hospital (AGH) has an internal anatomical materials approval process for the use of cadaveric tissues.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

K.B. and Q.Z. contributed equally to this work. K.B., Q.Z., A.H.A., D.T.A., B.C.C., and Z.L.W. conceived the experiments. K.B. and Q.Z. carried out the design and fabrication supervised by A.H.A. and Z.L.W.. K.B., Q.Z., I.S., K.H., and R.S. performed the experiments. K.B., Q.Z., A.H.A., Y.A., Z.L.W., and A.H.A. analyzed and interpreted the data. K.B., Q.Z., I.S., B.C.C., Y.A., and Z.L.W. wrote the manuscript and all the authors discussed the results and contributed to writing portions of the manuscript and editing the manuscript.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Keywords

bone healing, diagnostic, energy harvesting, medical implant, metamaterial, triboelectric nanogenerators

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