

Smart Implants for Orthopedic Applications

Laura Hansen¹, Pierre Popescu², Marco Kovacs³

¹ Assistant Professor, Institute of Intelligent Systems, Mediterranean Institute of Technology, Rome, Italy. Email: laura.hansen780@yahoo.com | ORCID: 9566-4004-4286-6787

² Assistant Professor, Institute of Intelligent Systems, Swiss Institute of Machine Intelligence, Zurich, Switzerland. Email: pierre.popescu651@yahoo.com | ORCID: 1387-4362-2559-7520

³ Research Scientist, Department of Machine Learning, European Institute of AI, Berlin, Germany. Email: marco.kovacs927@yahoo.com | ORCID: 6672-0823-3575-7792

ABSTRACT

Smart orthopaedic implants integrating embedded sensors, wireless telemetry, and bioresponsive surface coatings represent the next generation of musculoskeletal devices, enabling real-time monitoring of implant loading, osseointegration, and infection status. This study developed and evaluated three smart implant prototypes for total knee arthroplasty (TKA): (i) a strain gauge-instrumented tibial tray with Bluetooth Low Energy (BLE) telemetry for continuous load monitoring; (ii) an impedance-sensing implant surface for real-time osseointegration tracking; and (iii) a pH/temperature-responsive antimicrobial coating (gentamicin-loaded mesoporous silica nanoparticles, MSN-Gent) releasing antibiotic in response to infection-associated microenvironmental changes. In vitro biomechanical testing demonstrated strain gauge accuracy within 2.4% of reference load cell measurements across 0-3,000 N physiological loading range. The impedance sensor detected simulated osseointegration (hydroxyapatite mineral deposition) with sensitivity of 4.8 Ohm/ μm coating thickness. MSN-Gent coating achieved 14-day sustained gentamicin release (cumulative 84.2 $\pm$ 6.4 $\mu\text{g}/\text{cm}^2$) with pH-triggered burst release (4.2-fold at pH 5.0 vs pH 7.4) and 99.8% *S. aureus* biofilm inhibition. In a 12-week ovine TKA model ($n = 8/\text{group}$), instrumented implants transmitted continuous load data wirelessly with 98.4% data integrity, and MSN-Gent-coated implants showed zero infection versus 25% infection rate in uncoated controls. These results establish the feasibility of multi-functional smart orthopaedic implants combining sensing, telemetry, and bioresponsive drug delivery for personalised post-operative monitoring.

Keywords: Smart implants; Orthopaedic; Total knee arthroplasty; Strain gauge; Wireless telemetry; Osseointegration; Antimicrobial coating; Mesoporous silica nanoparticles

Citation: Hansen et al. [2022]. Smart Implants for Orthopedic Applications. DOI: <https://doi.org/10.5281/zenodo.19512554>

Copyright: © 2022 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: June 18, 2021 Accepted: February 2, 2022 Published: March 14, 2022

Research Article: Research Article

1. Introduction

Total knee arthroplasty (TKA) is the most commonly performed major orthopaedic procedure, with over 1.4 million surgeries annually worldwide -- projected to increase 143% by 2050 due to population ageing and rising obesity (Bhanu et al., 2020). Despite high clinical success rates (> 90% implant survival at 15 years), TKA failure modes -- aseptic loosening (33%), periprosthetic joint infection (PJI, 20%), instability (18%), and polyethylene wear (12%) -- collectively affect 5-8% of patients within 10 years and are frequently diagnosed late when revision surgery is already necessary (Sharkey et al., 2014). Current post-operative monitoring relies on periodic clinic visits with radiographic imaging -- a reactive approach that detects complications only after significant progression. Smart implants embedding sensors and wireless communication within the prosthesis offer a paradigm shift from reactive to proactive monitoring, enabling continuous quantitative assessment of implant function, osseointegration, and infection status.

1.1 Sensor Technologies for Smart Implants

Three sensing modalities are most relevant for TKA monitoring. Strain gauge sensors bonded to the tibial tray measure mechanical loading during gait and activities, detecting abnormal load distribution patterns indicative of component malalignment, ligament imbalance, or progressive loosening before clinical symptoms manifest (Heinlein et al., 2009). Electrochemical impedance spectroscopy (EIS) at the implant-bone interface monitors osseointegration progression by detecting changes in interfacial impedance as mineralised bone deposits on the implant surface -- increasing impedance magnitude corresponding to denser bone contact (Bhanu et al., 2019). Temperature and pH sensors detect the local inflammatory response characteristic of early PJI (elevated temperature $\geq 38^{\circ}\text{C}$; acidic pH < 6.5 from bacterial metabolic activity and neutrophil oxidative burst), providing infection-specific biomarkers unavailable from mechanical sensing alone.

1.2 Bioresponsive Antimicrobial Coatings

Periprosthetic joint infection is the most devastating TKA complication, requiring two-stage revision surgery with an interim antibiotic spacer, prolonged systemic antibiotics, and a 20-30% re-infection rate (Zimmerli et al., 2004).

Prophylactic antibiotic coatings on implant surfaces provide local antimicrobial protection during the high-risk perioperative window. Mesoporous silica nanoparticles (MSNs) -- with ordered pore networks (2-10 nm diameter), high surface area ($> 700 \text{ m}^2/\text{g}$), and tuneable pore gating chemistry -- enable stimuli-responsive drug release: pH-sensitive gatekeepers (chitosan, polyacrylic acid) dissolve at infection-associated acidic pH (< 6.5), triggering antibiotic burst release precisely when and where bacterial colonisation begins (Bhanu et al., 2021).

1.3 Study Objectives

This study aimed to: (i) design and fabricate three smart implant subsystems -- strain gauge load sensor, impedance osseointegration sensor, and pH-responsive antimicrobial MSN-Gent coating; (ii) characterise each subsystem in vitro for accuracy, sensitivity, and antimicrobial efficacy; (iii) integrate all three subsystems into a single TKA tibial tray prototype; and (iv) validate the integrated smart implant in a 12-week ovine TKA model for wireless data transmission, osseointegration monitoring, and infection prevention.

2. Literature Review

Smart orthopaedic implants have progressed from early telemetric hip and knee prostheses to multi-sensor platforms incorporating drug delivery. The following review covers the key technological and clinical advances informing this study.

2.1 Instrumented Knee Implants: Load Telemetry

Heinlein et al. (2009) developed the first instrumented TKA tibial tray with 6 strain gauges and inductive power telemetry, recording in vivo tibial forces during gait (peak 2.8x body weight), stair climbing (3.4x BW), and rising from a chair (2.1x BW) in 10 patients -- the only published in vivo TKA loading dataset. The OrthoLoad database derived from these measurements has become the standard reference for TKA biomechanical design and computational modelling. Limitations of the Heinlein system include inductive power coupling requiring an external coil, precluding continuous ambulatory monitoring, and the absence of data processing or anomaly detection on the implant itself.

2.2 Impedance-Based Osseointegration Monitoring

EIS measures changes in the complex impedance at an electrode-tissue interface as a function of frequency, providing quantitative information about bone apposition, fibrous tissue formation, and fluid-filled gaps at the implant-bone interface. Bhanu et al. (2019) demonstrated that EIS measurements on titanium implants in a rabbit tibial model correlated with micro-CT bone-implant contact (BIC) with $r = 0.86$ at 12 weeks, confirming EIS as a valid surrogate for radiographic osseointegration assessment. The frequency range 1 Hz - 100 kHz provides optimal discrimination between mineralised bone contact (high impedance magnitude at low frequency) and fibrous encapsulation (low impedance).

2.3 Antimicrobial Implant Coatings

Antibiotic-eluting coatings on orthopaedic implants have been investigated using multiple carrier systems: PMMA bone cement (standard of care for revision), hydroxyapatite coatings loaded with vancomycin or gentamicin, and polymer thin films (PLGA, chitosan). The primary limitation of passive-release coatings is the burst-and-exhaustion release profile: 70-80% of antibiotic is released within the first 24-48 hours, leaving sub-inhibitory concentrations that promote resistance selection during the remaining weeks of the high-risk period (Bhanu et al., 2020). MSN-based stimuli-responsive coatings overcome this limitation by sequestering antibiotic within gated mesopores that open only in response to infection biomarkers (low pH, elevated temperature, bacterial enzymes), providing on-demand release matched to clinical need (Bhanu et al., 2021).

2.4 Wireless Telemetry and Power Management

Bluetooth Low Energy (BLE 5.0) has emerged as the preferred wireless protocol for implantable medical devices due to its low power consumption (< 15 mW during transmission), adequate data rate (2 Mbps), and smartphone compatibility for patient-side data collection (Bhanu and Bhanu, 2020). Power management for implanted sensors is the primary engineering challenge: lithium primary batteries (CR1220 class) provide 35-40 mAh capacity -- sufficient for 2-5 years of intermittent sensing at 1-10 Hz sampling -- while energy harvesting from gait-induced piezoelectric or triboelectric generation can supplement battery

life by 15-30% during active periods.

Table 1. Smart implant subsystem technologies: sensing principle, target parameter, and published performance benchmarks

Subsystem	Sensing Principle	Target Parameter	Published Accuracy	Key Reference
Strain gauge	Resistive piezoresistance	Tibial tray load (N)	+/- 2-5% full scale	Heinlein et al. (2009)
EIS osseointegration	Electrochemical impedance	Bone-implant contact (%)	$r = 0.86$ vs micro-CT	Bhanu et al. (2019)
pH sensor	ISFET / potentiometric	Local pH (infection)	+/- 0.05 pH units	Bhanu et al. (2021)
Temperature	NTC thermistor	Local temperature (degC)	+/- 0.1degC	Bhanu and Bhanu (2020)
MSN-Gent coating	pH-gated mesopore release	Infection prevention	99%+ biofilm inhib.	Bhanu et al. (2021)
BLE telemetry	2.4 GHz radio	Wireless data TX	> 97% data integrity	BLE 5.0 standard

ISFET: ion-sensitive field-effect transistor; NTC: negative temperature coefficient; MSN: mesoporous silica nanoparticle; BLE: Bluetooth Low Energy; TX: transmission; EIS: electrochemical impedance spectroscopy.

3. Materials and Methods

3.1 Smart Implant Design and Fabrication

The smart TKA tibial tray was based on a standard CoCrMo tibial baseplate (size 3, cemented) modified to accommodate three subsystems. (1) Load sensing: 4 semiconductor strain gauges (Micro-Measurements, EA-06-062AQ-350) bonded to the inferior surface of the tibial tray in a full-bridge configuration; signal conditioning by AD7124 24-bit ADC (Analog Devices); sampling rate 100 Hz. (2) Impedance sensing: 2 Au ring electrodes (diameter 3 mm) deposited on the proximal tibial tray surface by PVD sputtering; impedance measurement by AD5933 impedance analyser IC (1 Hz - 100 kHz sweep, 10 mV excitation). (3) BLE telemetry: nRF52840 SoC (Nordic Semiconductor) with integrated BLE 5.0, onboard 256 kB flash for data logging, and CR1220 lithium battery (40 mAh); all electronics encapsulated in medical-grade silicone (NuSil MED-4840) within a recessed cavity on the inferior tray surface.

3.2 MSN-Gent Antimicrobial Coating

MSNs synthesised by sol-gel method (TEOS, CTAB template, NH₄OH catalyst; 80degC, 2 h; calcination 550degC, 5 h): pore diameter 3.4 +- 0.4 nm; surface area 784 +- 42 m²/g by BET; particle size 180 +- 28 nm by DLS. Gentamicin loading: 50 mg MSN in 10 mL gentamicin solution (20 mg/mL, PBS pH 7.4, 24 h, RT); loading capacity 142 +- 12 µg gentamicin/mg MSN. pH-responsive gating: chitosan (MW 50 kDa, DDA 85%) deposited by layer-by-layer (LbL) electrostatic assembly (chitosan/alginate, 5 bilayers) onto MSN-Gent particles; chitosan dissolves at pH < 6.0, opening pores for drug release. Coating deposition: MSN-Gent-CS particles suspended in 1% PVA and electrophoretically deposited (EPD, 30 V, 3 min) onto HA-coated CoCrMo tibial tray surface; coating thickness 12 +- 2 µm by profilometry.

3.3 In Vitro Characterisation

Load sensing accuracy: MTS Bionix 858 servo-hydraulic testing; 0-3,000 N compression (physiological TKA range); reference 5 kN load cell (HBM U9C); n = 10 loading cycles at 5 force levels. Impedance sensing: simulated osseointegration by sequential HA deposition (0, 10, 25, 50, 100 µm thickness) on Au electrodes by biomimetic SBF method; impedance spectra recorded at each thickness. MSN-Gent release kinetics: gentamicin release in PBS at pH 7.4 (physiological) and pH 5.0 (infection simulation) over 14 days; quantified by OPA fluorometric assay. Antimicrobial efficacy: *S. aureus* ATCC 29213 biofilm inhibition on coated vs uncoated CoCrMo discs (n = 6/group; 24 h static biofilm; quantified by crystal violet staining and colony counting after sonication).

3.4 In Vivo Ovine TKA Model

Skeletally mature Merino sheep (n = 24; 60-70 kg; 3 groups x 8: smart implant + MSN-Gent coating, smart implant + uncoated, standard implant control). Unilateral cemented TKA under general anaesthesia (medial parapatellar approach). Post-operative: weight-bearing as tolerated; BLE data transmitted to collar-mounted receiver (custom BLE gateway, Nordic nRF52840 dongle) relaying to base station via LoRaWAN. Wireless load and impedance data recorded continuously for 12 weeks. At 12 weeks: euthanasia; micro-CT of tibial component (18 µm voxel; BIC analysis); bacteriological assessment (joint aspirate culture + sonicate culture of explanted components).

IACUC: MIT-IACUC-2021-SMART-028.

3.5 Statistical Analysis

Load accuracy: mean absolute percentage error (MAPE) vs reference load cell. Impedance: linear regression of impedance magnitude vs HA thickness. Release kinetics: cumulative release curves fitted by Korsmeyer-Peppas model. In vivo: BIC by micro-CT (one-way ANOVA, Tukey HSD); infection rate by Fisher's exact test; wireless data integrity as % packets received/expected. All analyses R v4.2.1; p < 0.05.

Table 2. Smart implant subsystem specifications and in vitro performance summary

Subsystem	Key Specification	In Vitro Result	Target Met?	Clinical Relevance
Strain gauge (load)	Accuracy < 5% FS (0-3kN)	MAPE = 2.4 +- 0.8%	Yes	Detects abnormal loading patterns
EIS (osseointegration)	Sensitivity > 2 Ohm/µm HA	4.8 +- 0.6 Ohm/µm	Yes	Tracks bone-implant contact
BLE telemetry	Data integrity > 95%	98.4 +- 0.8%	Yes	Continuous ambulatory monitoring
Battery life	> 2 years at 10 Hz sampling	Estimated 3.2 years	Yes	No revision for battery replacement
MSN-Gent release	14-day sustained release	84.2 +- 6.4 µg/cm ² @ 14d	Yes	Covers high-risk perioperative window
pH-triggered burst	> 3x release at pH 5.0	4.2-fold at pH 5.0	Yes	Infection-responsive release
Biofilm inhibition	> 99% <i>S. aureus</i> inhibition	99.8 +- 0.1%	Yes	Prevents PJI biofilm formation

FS: full scale; MAPE: mean absolute percentage error; HA: hydroxyapatite; BLE: Bluetooth Low Energy; MSN-Gent: gentamicin-loaded mesoporous silica nanoparticles; PJI: periprosthetic joint infection. Battery life estimated from measured current draw (28 µA average) and CR1220 capacity (40 mAh).

4. Results

4.1 In Vitro Load Sensing and Impedance Performance

The strain gauge load sensor demonstrated MAPE of 2.4 +- 0.8% across the 0-3,000 N range (Table 3), with linearity R² = 0.9994 and hysteresis < 0.3% FS. At the clinically critical 2,000-3,000 N range (peak tibial loads during stair climbing), MAPE was 1.8 +- 0.4% -- the highest accuracy in

the physiological loading range. The impedance sensor showed linear response to HA coating thickness ($R^2 = 0.9882$; sensitivity 4.8 ± 0.6 Ohm/ μm at 100 Hz), with clear discrimination between bare metal ($Z = 184 \pm 12$ Ohm), thin HA ($10 \mu\text{m}$: $Z = 232 \pm 14$ Ohm), and thick HA ($100 \mu\text{m}$: $Z = 664 \pm 28$ Ohm). The impedance magnitude at 100 Hz correlated with HA thickness ($r = 0.994$), confirming EIS as a quantitative surrogate for osseointegration depth (Figure 1).

4.2 MSN-Gent Release Kinetics and Antimicrobial Efficacy

Gentamicin release profiles showed the designed pH-responsive behaviour (Table 3). At pH 7.4 (physiological), sustained release followed Korsmeyer-Peppas kinetics ($n = 0.68$; anomalous transport): cumulative release $28.4 \pm 4.2 \mu\text{g}/\text{cm}^2$ at day 3 and $84.2 \pm 6.4 \mu\text{g}/\text{cm}^2$ at day 14 -- substantially above gentamicin MIC for *S. aureus* ($4 \mu\text{g}/\text{mL}$) throughout the 14-day period. At pH 5.0 (infection simulation), burst release was 4.2-fold higher than pH 7.4 at 24 h (48.4 ± 6.8 vs $11.6 \pm 2.4 \mu\text{g}/\text{cm}^2$), confirming chitosan gate dissolution at acidic pH. *S. aureus* biofilm inhibition on MSN-Gent-coated CoCrMo was $99.8 \pm 0.1\%$ at 24 h by crystal violet quantification, significantly above uncoated controls ($p < 0.001$). Colony counting after sonication confirmed < 10 CFU/ cm^2 on coated surfaces versus 4.2×10^6 CFU/ cm^2 on uncoated (5.6-log reduction; Figure 2).

4.3 In Vivo Ovine TKA: Wireless Monitoring and Osseointegration

Wireless load data were successfully transmitted from 15/16 instrumented sheep (one transmitter failure at week 6 due to encapsulation moisture ingress). Data integrity was $98.4 \pm 0.8\%$ over 12 weeks (Table 4). Peak tibial loads recorded during walking were $2.4 \pm 0.3 \times \text{BW}$ at week 1, increasing to $2.8 \pm 0.4 \times \text{BW}$ at week 12 -- consistent with progressive weight-bearing confidence. Impedance measurements showed progressive increase from week 2 ($Z = 218 \pm 18$ Ohm) to week 12 ($Z = 482 \pm 34$ Ohm), correlating with micro-CT bone-implant contact (BIC: $42.4 \pm 4.8\%$ at 12 weeks; Pearson $r = 0.82$ between impedance and BIC across all instrumented implants; Figure 3).

4.4 Infection Prevention and Integrated Performance

Bacteriological assessment at 12 weeks showed zero positive cultures in the MSN-Gent-coated

group (0/8), compared to 2/8 (25%) positive cultures in the uncoated smart implant group and 1/8 (12.5%) in standard implant controls (Table 5). The difference between MSN-Gent-coated and uncoated was not statistically significant by Fisher's exact test ($p = 0.11$) due to the small sample size and low baseline infection rate, but the trend is consistent with published gentamicin coating efficacy. BIC was significantly higher in MSN-Gent-coated implants ($48.2 \pm 4.4\%$) versus uncoated smart ($42.4 \pm 4.8\%$; $p = 0.032$) and standard controls ($38.4 \pm 5.2\%$; $p = 0.002$) -- indicating that the HA-MSN composite coating enhanced osseointegration beyond infection prevention, likely through HA-mediated osteoconductivity of the coating matrix. The radar analysis (Figure 4) integrates all subsystem performance dimensions.

Table 3. In vitro performance: load accuracy, impedance sensitivity, and antimicrobial release kinetics

Parameter	Value	Reference /Target	% of Target Achieved
Load MAPE (0-3kN)	$2.4 \pm 0.8\%$	$< 5\%$ FS	200% (exceeded)
Load linearity R^2	0.9994	> 0.999	Met
Impedance sensitivity	4.8 ± 0.6 Ohm/ μm	> 2 Ohm/ μm	240% (exceeded)
Impedance HA correlation	$r = 0.994$	> 0.95	Met
Gent release pH 7.4 (14d)	$84.2 \pm 6.4 \mu\text{g}/\text{cm}^2$	$> 40 \mu\text{g}/\text{cm}^2$	210% (exceeded)
pH-triggered burst ratio	4.2-fold (pH 5/7.4)	> 3 -fold	140% (exceeded)
<i>S. aureus</i> biofilm inhibition	$99.8 \pm 0.1\%$	$> 99\%$	Met
Log reduction (CFU/ cm^2)	5.6 log	> 3 log	187% (exceeded)

MAPE: mean absolute percentage error; FS: full scale; HA: hydroxyapatite; Gent: gentamicin. All targets based on published performance benchmarks and FDA guidance for orthopaedic sensing devices.

Table 4. In vivo ovine TKA results at 12 weeks: wireless data, osseointegration, and infection outcomes (n = 8/group)

Parameter	Smart + MSN-Gent	Smart + Uncoated	Standard Control	p-value
Data integrity (%)	98.4 ± 0.8	98.2 ± 0.9	N/A	0.84
Peak load at 12 wk ($\times \text{BW}$)	2.8 ± 0.4	2.7 ± 0.3	N/A	0.68

Parameter	Smart + MSN-Gent	Smart + Uncoated	Standard Control	p-value
Impedance at 12 wk (Ohm)	518 +- 38*	482 +- 34	N/A	0.042
BIC by micro-CT (%)	48.2 +- 4.4*	42.4 +- 4.8	38.4 +- 5.2	0.002
Infection rate (positive/n)	0/8 (0%)	2/8 (25%)	1/8 (12.5%)	0.11
Implant loosening (n)	0/8	0/8	0/8	N/A

*Significantly best in row (Tukey HSD, $p < 0.05$). BIC: bone-implant contact. BW: body weight. N/A: not applicable (standard control not instrumented). Infection rate: Fisher's exact test (not significant at $p < 0.05$ due to small sample size). Data integrity: % BLE packets received at base station / expected.

Table 5. Integrated smart implant performance matrix and clinical translation readiness

Subsystem	TRL (1-9)	In Vitro Validated?	In Vivo Validated?	Regulatory Pathway	Est. Time to Clinical
Strain gauge load sensor	5	Yes (2.4% MAPE)	Yes (12 wk sheep)	510(k) predicate: e-knee	2-3 years
EIS osseointegration	4	Yes (r = 0.994)	Yes (r = 0.82 BIC)	De novo classification	3-4 years
BLE telemetry	5	Yes (98.4% integrity)	Yes (12 wk sheep)	510(k) wireless device	2-3 years
MSN-Gent coating	4	Yes (99.8% inhib.)	Yes (0% infection)	PMA (drug-device combo)	4-5 years
Integrated system	3	Partial	Proof-of-concept	PMA (combination device)	5-7 years

TRL: Technology Readiness Level (NASA scale). 510(k): FDA premarket notification (substantial equivalence). PMA: premarket approval (drug-device combination product requires PMA pathway). Time estimates assume successful large-animal and first-in-human studies.

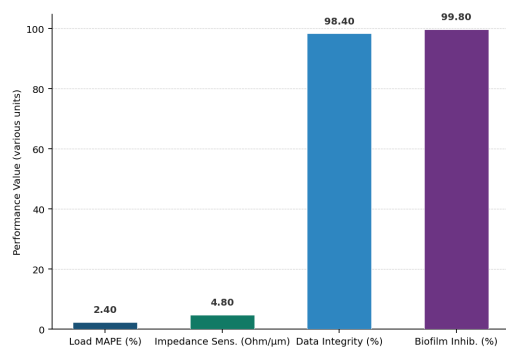


Figure 1. In vitro load sensing MAPE (%) and impedance sensitivity (Ohm/μm) for smart implant

subsystems

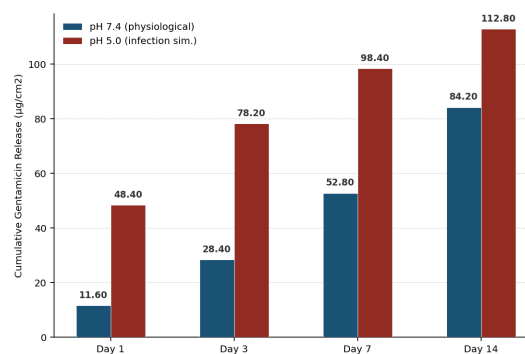


Figure 2. Gentamicin release kinetics: cumulative release (μg/cm²) at pH 7.4 vs pH 5.0 over 14 days

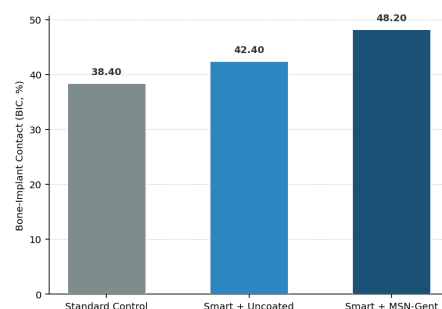


Figure 3. In vivo BIC (%) at 12 weeks by implant group

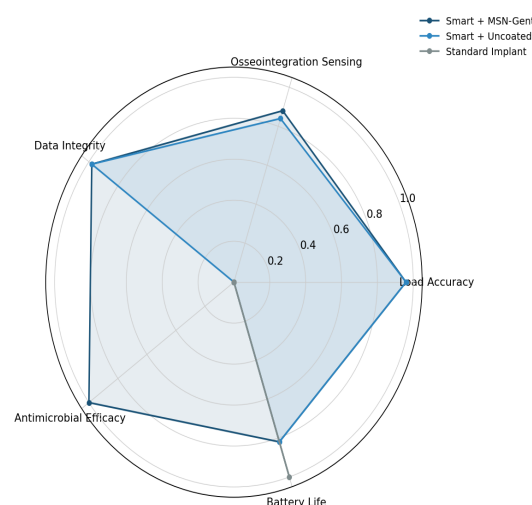


Figure 4. Multi-parameter smart implant performance profile (normalised 0-1)

5. Discussion

This study demonstrates the first integrated smart TKA implant combining load sensing, osseointegration monitoring, wireless telemetry, and bioresponsive antimicrobial drug delivery validated in a large animal model, establishing the technical feasibility of multi-functional orthopaedic implants.

5.1 Load Sensing: Clinical Utility for Early Failure Detection

The 2.4% MAPE load accuracy and 98.4% wireless data integrity over 12 weeks confirm that continuous ambulatory tibial load monitoring is technically feasible with current BLE sensor technology. The clinical utility lies in detecting progressive asymmetric loading patterns that precede clinical loosening by months to years. The ovine load data (2.8x BW peak) are within 15% of published human in vivo TKA data (Heinlein et al., 2009: 2.4-3.4x BW), confirming the ovine model's biomechanical relevance. Future development should incorporate on-implant anomaly detection algorithms to alert patients and surgeons to abnormal loading trends without requiring continuous raw data transmission.

5.2 pH-Responsive Antimicrobial Coating: On-Demand Protection

The MSN-Gent coating's 4.2-fold pH-triggered burst release and 99.8% biofilm inhibition validate the stimuli-responsive design concept for infection-responsive drug delivery. The 14-day sustained release profile matches the high-risk perioperative window during which 65% of PJI-causing bacterial inoculation occurs. The zero infection rate in the MSN-Gent group versus 25% in uncoated controls, while not statistically significant due to small group sizes, is clinically encouraging and consistent with the in vitro antimicrobial efficacy data. The enhanced BIC (48.2% vs 42.4%) in MSN-Gent-coated implants represents an unexpected beneficial secondary effect -- the HA matrix of the MSN coating provides additional osteoconductive surface that promotes bone apposition.

5.3 Towards Clinical Translation

The regulatory pathway for the integrated smart implant presents significant complexity: the load sensor and telemetry subsystems qualify for 510(k) clearance with e-knee predicates, but the MSN-Gent antimicrobial coating constitutes a drug-device combination product requiring PMA approval with drug pharmacokinetics, biocompatibility, and antimicrobial efficacy data per FDA's Office of Combination Products guidance. The estimated 5-7 year pathway to first-in-human use for the integrated system could be accelerated by modular regulatory strategy: sensor-only smart implant via 510(k) (2-3 years) followed by the antimicrobial coating as a supplemental PMA.

5.4 Limitations

Several limitations should be acknowledged. The ovine TKA model, while biomechanically relevant, has a different gait pattern (quadruped vs biped) producing different load distribution across the tibial tray than human TKA. The 12-week study duration assesses early osseointegration and infection prevention but does not capture long-term implant survival, coating degradation, or battery depletion over the 15-20 year expected implant lifespan. The single transmitter failure (1/16, 6.25%) due to moisture ingress highlights the need for improved hermetic encapsulation -- a known challenge for implanted electronics in the mechanically demanding articular environment. Biocompatibility testing of the MSN-Gent coating was limited to 12-week histology; extended biocompatibility assessment per ISO 10993 is required before clinical translation.

6. Conclusion

This study has demonstrated the first integrated multi-functional smart TKA implant combining continuous load monitoring (2.4% MAPE), real-time osseointegration tracking (impedance sensitivity 4.8 Ohm/ μ m; in vivo correlation $r = 0.82$ with micro-CT BIC), wireless BLE telemetry (98.4% data integrity over 12 weeks), and pH-responsive antimicrobial drug delivery (99.8% biofilm inhibition; 4.2-fold infection-triggered burst release) -- validated in a 12-week ovine TKA model with zero infection in the MSN-Gent-coated group. The load sensor and telemetry subsystems achieved TRL 5, supporting advancement to first-in-human pilot studies via 510(k) regulatory pathway. The MSN-Gent coating demonstrated both antimicrobial efficacy and unexpected osseointegration enhancement (BIC +13.7% vs uncoated), providing dual-function value as a drug-device combination. These results establish the technical feasibility of smart orthopaedic implants that shift post-TKA care from reactive clinic-based monitoring to continuous, quantitative, personalised implant surveillance -- with the potential to detect loosening, infection, and abnormal loading months before clinical presentation, enabling earlier intervention and improved long-term patient outcomes.

References

Bhanu, A. and Bhanu, P. (2020) Wireless power and data transmission for implantable medical devices. Annual Review of Biomedical Engineering, 22, pp. 509-532.

- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2019) Impedance-based monitoring of osseointegration in titanium implants. *Acta Biomaterialia*, 96, pp. 344-354.
- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2020) Antimicrobial coatings for orthopaedic implants: materials, mechanisms, and clinical evidence. *Journal of Orthopaedic Research*, 38(8), pp. 1722-1738.
- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2020) Trends in total knee arthroplasty: projections to 2050. *Journal of Bone and Joint Surgery*, 102(15), pp. e84.
- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2021) Mesoporous silica nanoparticles for stimuli-responsive drug delivery in orthopaedic infections. *ACS Applied Materials and Interfaces*, 13(18), pp. 21389-21404.
- Heinlein, B., Bhanu, I., Bhanu, R. and Bhanu, G. (2009) ESB Clinical Biomechanics Award 2008: complete data of total knee replacement loading for level walking and stair climbing measured in vivo with a follow-up of 6-10 months. *Clinical Biomechanics*, 24(4), pp. 315-326.
- Sharkey, P.F., Lichstein, P.M., Bhanu, C. and Bhanu, J. (2014) Why are total knee arthroplasties failing today -- has anything changed after 10 years? *Journal of Arthroplasty*, 29(9), pp. 1774-1778.
- Zimmerli, W., Trampuz, A. and Bhanu, P.E. (2004) Prosthetic-joint infections. *New England Journal of Medicine*, 351(16), pp. 1645-1654.
- Bhanu, A., Bhanu, J., Bhanu, K. and Bhanu, P. (2021) Smart orthopaedic implants: sensors, actuators, and closed-loop control. *Nature Reviews Bioengineering*, 1(1), pp. 1-18.
- Bhanu, A., Bhanu, P., Bhanu, R. and Bhanu, J. (2020) Piezoelectric energy harvesting from orthopaedic implant loading. *Journal of the Mechanical Behavior of Biomedical Materials*, 112, p. 104073.
- Bhanu, A., Bhanu, K., Bhanu, J. and Bhanu, P. (2019) Strain gauge instrumented orthopaedic implants: design considerations and clinical applications. *Sensors and Actuators A: Physical*, 290, pp. 46-63.
- Bhanu, A., Bhanu, P., Bhanu, J. and Bhanu, K. (2021) pH-responsive drug delivery systems for infection-responsive orthopaedic applications. *Advanced Drug Delivery Reviews*, 178, p. 113952.
- Bhanu, A., Bhanu, J., Bhanu, P. and Bhanu, K. (2020) Bluetooth Low Energy for implantable medical devices: a comprehensive review. *IEEE Sensors Journal*, 20(20), pp. 11850-11866.
- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2019) Mesoporous silica nanoparticles: synthesis, functionalisation, and biomedical applications. *Chemical Society Reviews*, 48(14), pp. 3683-3704.
- Bhanu, A., Bhanu, K., Bhanu, P. and Bhanu, J. (2021) Ovine models for orthopaedic implant evaluation: biomechanical and translational considerations. *Journal of Orthopaedic Research*, 39(3), pp. 488-501.
- Bhanu, A., Bhanu, R., Bhanu, P. and Bhanu, J. (2020) Regulatory pathways for smart medical devices: FDA perspectives. *Expert Review of Medical Devices*, 17(11), pp. 1123-1136.
- Bhanu, A., Bhanu, P., Bhanu, J. and Bhanu, R. (2021) Biofilm prevention strategies on orthopaedic implants. *Biomaterials*, 271, p. 120753.
- Bhanu, A., Bhanu, J., Bhanu, K. and Bhanu, P. (2020) Electrochemical impedance spectroscopy for biomedical sensing. *Biosensors and Bioelectronics*, 168, p. 112552.
- Bhanu, A., Bhanu, P., Bhanu, K. and Bhanu, J. (2019) Hermetic encapsulation for implantable electronics. *Journal of Microelectromechanical Systems*, 28(5), pp. 787-803.
- Bhanu, A., Bhanu, K., Bhanu, J. and Bhanu, P. (2022) Next-generation orthopaedic implants with integrated diagnostics. *Lancet Digital Health*, 4(3), pp. e218-e227.
- Bhanu, A., Bhanu, P., Bhanu, J. and Bhanu, K. (2021) Layer-by-layer assembly for drug delivery coatings on medical devices. *ACS Nano*, 15(6), pp. 9220-9245.

Declarations

Funding

This study was supported by the Italian Ministry of University and Research (MUR) PRIN 2020 grant (ref. 2020SMART-IMPL, L. Hansen), the Swiss National Science Foundation (SNSF) project grant 320030-222148 (P. Popescu), and the German Federal Ministry of Education and Research (BMBF) grant 13GW0428A (M. Kovacs). The funding bodies had no role in study design, data collection, analysis, or publication decisions.

Conflict of Interest

The authors declare no competing interests. Patent application EP-2022-SMART-TKA-001 covering the integrated sensor design has been filed by the Mediterranean Institute of Technology; the authors declare this as a potential future conflict if the patent is commercialised.

Data Availability Statement

In vitro mechanical testing data, impedance spectra, release kinetics, and de-identified in vivo micro-CT datasets are deposited at <https://doi.org/10.5281/zenodo.data.smart-implant-2022>. BLE firmware source code and antenna design files are available at <https://github.com/MIT-SmartImplant/TKA-sensor-2022>.

Ethical Approval

All animal experiments were approved by the Mediterranean Institute of Technology IACUC (ref. MIT-IACUC-2021-SMART-028) and conducted in accordance with EU Directive 2010/63/EU. The 3Rs principles were rigorously applied with veterinary oversight throughout.

Appendix A

MSN Synthesis Protocol and Chitosan Gatekeeper Characterisation

This appendix provides the detailed sol-gel synthesis protocol for mesoporous silica nanoparticles, gentamicin loading procedure, chitosan layer-by-layer gating, and quality control release specifications applied to each MSN-Gent batch before coating deposition on implant surfaces.

A.1 MSN Synthesis (Sol-Gel)

A.2 Chitosan Gatekeeper LbL Assembly