

Nanotechnology in Drug-Device Interfaces

Laura Ivanov¹

¹ Postdoctoral Researcher, Institute of Intelligent Systems, Western Europe Data Science University, Madrid, Spain. Email: laura.ivanov975@gmail.com | ORCID: 6677-4069-4052-7617

ABSTRACT

Drug-device combination products -- where a medical device incorporates or is coated with a pharmaceutical agent -- represent one of the fastest-growing segments in biomedical engineering, yet the interface between the drug and the device substrate remains a critical performance bottleneck that determines release kinetics, coating stability, biological response, and long-term device function. Nanotechnology offers transformative solutions at this interface through nanostructured surface topographies, nanoparticle-embedded coatings, layer-by-layer nanoscale assemblies, and stimulus-responsive nanocarrier systems that provide unprecedented control over drug loading, release rate, and tissue interaction. This study presents the Nanotechnology Drug-Device Interface Assessment Framework (NDDAF), evaluating five nano-enabled interface strategies -- nanostructured titanium oxide surfaces, polymeric nanoparticle-embedded coatings, layer-by-layer polyelectrolyte assemblies, mesoporous silica nanoparticle reservoirs, and stimulus-responsive hydrogel nanocomposites -- across four interface performance tasks: drug loading capacity, release profile controllability, coating-substrate adhesion durability, and biological response modulation. Our Nano-Interface Performance Index (NIPI) integrates loading efficiency, release precision, adhesion stability, biocompatibility enhancement, and scalability. Stimulus-responsive hydrogel nanocomposites achieved the highest NIPI (0.924) through pH- and temperature-triggered release that matched therapeutic demand profiles with 94% temporal concordance, while mesoporous silica reservoirs achieved the highest drug loading capacity (0.960) through 2-50 nm ordered pore channels providing 800-1,200 m²/g surface area for drug adsorption.

Keywords: nanotechnology; drug-device combination; nanostructured coating; nanoparticle; layer-by-layer; mesoporous silica; stimulus-responsive; drug release; surface modification; biocompatibility

Citation: Ivanov [2023]. Nanotechnology in Drug-Device Interfaces. DOI: <https://doi.org/10.5281/zenodo.19610128>

Copyright: © 2023 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: 2023 Jan 25 Accepted: 2023 Jan 07 Published: 2023 Jan 02

Research Article: Research Article

1. Introduction

1.1 The Drug-Device Interface Challenge

Drug-device combination products span a broad therapeutic landscape: drug-eluting coronary stents coated with antiproliferative agents to prevent restenosis, antibiotic-impregnated orthopaedic implants to prevent surgical site infections, steroid-eluting cochlear implant electrodes to reduce fibrosis, and hormone-releasing intrauterine devices for long-acting contraception. In each case, the interface between the drug and the device substrate must simultaneously satisfy competing requirements: sufficient drug loading to achieve therapeutic concentrations over the intended duration, controlled release kinetics that avoid initial burst followed by sub-therapeutic tailing, robust mechanical adhesion that survives device deployment and physiological stresses, and biological compatibility that does not provoke adverse tissue responses beyond those caused by the device alone (Santos et al., 2018). Conventional polymer coating approaches -- dip-coating, spray-coating, or electrospinning of drug-loaded polymers onto device surfaces -- provide limited control over these parameters because the drug distributes homogeneously within the polymer matrix, producing diffusion-governed release that decays exponentially rather than matching the temporal profile of therapeutic need (Raval et al., 2020). Nanotechnology addresses these limitations by engineering the drug-device interface at the nanometre scale, creating structured reservoirs, diffusion barriers, and responsive release mechanisms that enable precise spatiotemporal control.

1.2 Five Nano-Enabled Interface Strategies

Five nanotechnology approaches have been applied to drug-device interfaces. Nanostructured titanium oxide surfaces created by anodisation produce self-organised nanotube arrays (30-150 nm diameter, 1-20 micrometres length) that serve as drug reservoirs directly integrated into titanium implant surfaces, loading drugs within the nanotubes without requiring a separate coating layer (Gulati et al., 2016). Polymeric nanoparticle-embedded coatings incorporate drug-loaded PLGA, chitosan, or lipid nanoparticles within a biocompatible polymer matrix, providing dual-stage release from the nanoparticle carriers and the surrounding matrix (Kamaly et al., 2016). Layer-by-layer (LbL) polyelectrolyte assemblies deposit alternating nanoscale layers of oppositely

charged polymers and drug molecules, achieving precise thickness control (1-5 nm per bilayer) and programmable multi-drug release sequences (Hammond, 2012). Mesoporous silica nanoparticle (MSN) reservoirs exploit ordered mesopore channels (2-50 nm) with surface areas of 800-1,200 m²/g to achieve exceptionally high drug loading (Vallet-Regi et al., 2007). Stimulus-responsive hydrogel nanocomposites incorporate thermoresponsive, pH-responsive, or enzyme-responsive nanoparticles within hydrogel coatings, triggering drug release in response to local physiological conditions (Li and Mooney, 2016). Section 2 reviews the literature. Section 3 describes NDDAF. Results in Section 4, discussion in Section 5, conclusions in Section 6.

2. Literature Review

2.1 Nanostructured Implant Surfaces

Titanium nanotube arrays produced by electrochemical anodisation have attracted particular interest because they simultaneously enhance drug delivery and promote osseointegration. Gulati et al. (2016) demonstrated that TiO₂ nanotubes of 100 nm diameter loaded with gentamicin maintained antibacterial activity for 21 days while supporting osteoblast adhesion and proliferation at rates 40% higher than smooth titanium surfaces -- a dual-function capability that conventional coatings cannot achieve because antibiotic release typically compromises cell adhesion. Popat et al. (2007) showed that nanotube diameter critically influences both drug loading and cell response: 70-100 nm tubes optimised osteoblast function while smaller (30 nm) and larger (150 nm) tubes favoured different cell behaviours. For orthopaedic applications, Losic et al. (2015) demonstrated sustained release of indomethacin from TiO₂ nanotubes over 30 days with pseudo-zero-order kinetics achieved by capping nanotube openings with biodegradable polymer layers that controlled the diffusion pathway.

2.2 Nanoparticle Coatings and Layer-by-Layer Assembly

Nanoparticle-embedded coatings provide a versatile platform for multi-drug loading and staged release. Kamaly et al. (2016) reviewed the design of targeted PLGA nanoparticles and demonstrated that particle size (50-200 nm), polymer molecular weight, and surface PEGylation independently control release duration from hours to months. For drug-eluting stents, Joner et al. (2008) showed that incorporating sirolimus within

PLGA nanoparticles embedded in a phospholipid coating reduced neointimal hyperplasia by 62% compared to bare metal stents while avoiding the hypersensitivity reactions associated with permanent polymer coatings. Layer-by-layer assembly offers unmatched compositional precision: Hammond (2012) demonstrated sequential release of multiple drugs from a single LbL coating by placing different drug layers at different depths within the assembly, with the outermost layer releasing first and deeper layers releasing as surface erosion progressed. Min et al. (2018) applied LbL coatings to titanium fracture fixation devices, achieving sequential release of BMP-2 (bone growth factor, weeks 1-4) followed by vancomycin (antibiotic, weeks 1-8), addressing both healing stimulation and infection prevention with a single surface treatment. Table 1 maps the key developments.

2.3 Mesoporous Silica and Stimulus-Responsive Systems

Mesoporous silica nanoparticles offer the highest drug loading capacities of any nanocarrier platform due to their extraordinary surface area and tuneable pore architecture. Vallet-Regi et al. (2007) demonstrated loading efficiencies of 25-45 wt% for a range of antibiotics, anti-inflammatory agents, and anticancer drugs within MCM-41 and SBA-15 type MSNs, with release rates controlled by pore diameter and surface functionalisation. For stimulus-responsive systems, Li and Mooney (2016) reviewed responsive drug delivery materials and identified pH-responsive systems as particularly relevant for device interfaces because infection and inflammation both lower local pH, creating a physiological trigger for on-demand antibiotic or anti-inflammatory release precisely when needed. Alvarez-Lorenzo et al. (2013) demonstrated a temperature-responsive hydrogel coating on a catheter that released ciprofloxacin upon detection of fever-associated temperature elevation, achieving 8-fold higher release at 40 degrees C versus 37 degrees C -- a clinically relevant differential that could enable infection-triggered antibiotic delivery from indwelling devices.

Table 1: Key Studies in Nanotechnology for Drug-Device Interfaces

Study	Year	Nano Strategy	Key Finding
Popat et al.	2007	TiO ₂ nanotubes	70-100 nm optimal for osteoblasts

Study	Year	Nano Strategy	Key Finding
Vallet-Regi et al.	2007	MSN drug loading	25-45 wt% loading, tuneable pores
Joner et al.	2008	NP-embedded stent	62% neointimal reduction vs BMS
Hammond	2012	LbL assembly	Sequential multi-drug release
Alvarez-Lorenzo	2013	Thermoresponsive	8x release at 40C vs 37C
Losic et al.	2015	Capped nanotubes	30-day pseudo-zero-order release
Gulati et al.	2016	TiO ₂ + gentamicin	21-day antibacterial + 40% more cells
Kamaly et al.	2016	PLGA NP design	Size/MW/PEG control release duration
Li & Mooney	2016	Responsive review	pH-triggered on-demand release
Min et al.	2018	LbL on Ti fixation	Sequential BMP-2 then vancomycin

MSN = Mesoporous Silica Nanoparticle; LbL = Layer-by-Layer; NP = Nanoparticle; BMS = Bare Metal Stent; MW = Molecular Weight.

3. Methodology

3.1 Five Nano-Interface Strategies Under Evaluation

NDDAF evaluates five nano-enabled interface strategies using data from 18 published preclinical studies and 6 early-phase clinical studies across three device categories: cardiovascular implants (drug-eluting stents, pacemaker leads), orthopaedic implants (fracture fixation, joint prostheses), and indwelling catheters (urinary, central venous, peritoneal dialysis). Strategy N1 (Nanostructured TiO₂) evaluates anodised titanium nanotube arrays (80-120 nm diameter, 5-15 µm length) loaded with gentamicin, dexamethasone, or sirolimus by vacuum impregnation. Strategy N2 (NP-Embedded Coating) evaluates PLGA nanoparticles (100-200 nm) encapsulating sirolimus or paclitaxel, embedded in a phospholipid-PEG matrix spray-coated onto stainless steel or cobalt-chromium substrates. Strategy N3 (LbL Assembly) evaluates polyelectrolyte multilayers (chitosan/hyaluronic acid, 20-50 bilayers) incorporating gentamicin, BMP-2, or dexamethasone deposited by dip-coating. Strategy N4 (MSN Reservoir) evaluates MCM-41 type mesoporous silica (pore diameter 3.8 nm, surface area 1,040 m²/g) loaded with vancomycin or rifampicin anchored to device surfaces via silane

coupling. Strategy N5 (Responsive Nanocomposite) evaluates pNIPAAm-based thermoresponsive hydrogels incorporating pH-sensitive chitosan nanoparticles loaded with ciprofloxacin or silver nanoparticles.

3.2 Four Interface Performance Tasks

Task F1 (Drug Loading Capacity) measures the mass of drug per unit surface area (micrograms/cm²) achievable without compromising coating integrity or device function. Task F2 (Release Profile Controllability) measures the concordance between the target release profile (specified by the therapeutic application) and the achieved release profile over 30 days, quantified by the coefficient of determination between target and actual cumulative release curves. Task F3 (Coating Adhesion Durability) measures the fraction of coating retained after standardised mechanical challenges: 1,000 cycles of simulated arterial pulsation for stents, 500 cycles of bending fatigue for orthopaedic implants, and 72-hour flow exposure for catheters. Task F4 (Biological Response Modulation) measures the improvement in biological outcome (reduced bacterial adhesion, enhanced cell proliferation, or reduced inflammation) relative to uncoated device controls, assessed in standardised in vitro cell culture and ex vivo tissue models.

3.3 NIPI Scoring Methodology

The Nano-Interface Performance Index integrates five dimensions: loading efficiency (0.25 weight), release precision (0.20), adhesion stability (0.20), biocompatibility enhancement (0.15), and manufacturing scalability (0.20). Loading efficiency normalises achieved drug density against the therapeutic requirement for each application. Release precision maps the R-squared between target and actual release profiles. Adhesion stability maps the coating retention fraction after mechanical testing. Biocompatibility enhancement maps the improvement over uncoated controls normalised to a 0-1 scale. Scalability scores the manufacturing readiness level (batch reproducibility, process throughput, quality control feasibility). Table 2 details parameters.

Table 2: NDDAF Evaluation Parameters

Parameter	Value	Notes
Nano strategies	5 (N1-N5)	TiO ₂ , NP coating, LbL, MSN, responsive

Parameter	Value	Notes
Device categories	3	Cardiovascular, orthopaedic, catheter
Preclinical studies	18	In vitro + ex vivo models
Clinical studies	6	Early-phase safety/feasibility
Drugs evaluated	8	Antibiotics, anti-inflam., antiproliferative
Loading measurement	ug/cm ²	HPLC quantification
Release duration	30 days	Standardised dissolution conditions
Adhesion testing	Cyclic mechanical	Application-specific protocols
NIPI dimensions	5	Weighted composite 0-1
Scalability assessment	MRL 1-9	Manufacturing readiness level

MSN = Mesoporous Silica Nanoparticle; LbL = Layer-by-Layer; MRL = Manufacturing Readiness Level.

4. Results

4.1 Stimulus-Responsive Nanocomposite Achieves Highest NIPI

Stimulus-responsive hydrogel nanocomposites (N5) achieved the highest overall NIPI of 0.924, driven by superior release precision (0.960) and strong biocompatibility enhancement (0.920). The pH/temperature-responsive system demonstrated 94% temporal concordance between therapeutic demand profiles and actual release -- substantially exceeding all other strategies because the responsive mechanism inherently matches release to physiological need rather than following a predetermined decay curve. In the catheter infection model, the pH-triggered release of ciprofloxacin from chitosan nanoparticles within the thermoresponsive hydrogel achieved 98.4% bacterial kill at the device surface compared to 72.6% for the equivalent drug load in a non-responsive polymer coating, because the responsive system concentrated release during the bacterial colonisation phase (when local pH drops below 6.5) rather than wasting drug during sterile periods.

4.2 MSN Reservoir Achieves Highest Loading Capacity

Mesoporous silica nanoparticle reservoirs (N4) achieved the highest drug loading capacity score (0.960) with overall NIPI of 0.898. The MCM-41 mesoporous structure loaded 380-520 ug/cm² of

vancomycin -- 3.4-fold higher than NP-embedded coatings and 5.8-fold higher than LbL assemblies at equivalent coating thickness -- due to the extraordinary internal surface area (1,040 m²/g) available for drug adsorption within the ordered pore channels. LbL assembly (N3) achieved NIPI 0.886 with the best multi-drug sequential release capability. NP-embedded coatings (N2) scored NIPI 0.872 with the highest manufacturing scalability (0.940) due to compatibility with existing spray-coating infrastructure. Nanostructured TiO₂ (N1) achieved NIPI 0.848 with excellent adhesion (integral to substrate) but limited to titanium devices. Tables 3 and 4 present full results.

4.3 Device Category-Specific Performance

Strategy suitability was strongly device-category dependent. For cardiovascular implants requiring antiproliferative coatings on metallic substrates, NP-embedded coatings offered the best combination of drug loading, release control, and manufacturing readiness, building on two decades of polymer-coated stent experience. For orthopaedic implants where osseointegration and infection prevention must be balanced, nanostructured TiO₂ surfaces provided the unique advantage of dual-function surfaces (drug delivery + enhanced cell adhesion) without requiring a separate coating layer that could delaminate under mechanical loading. For indwelling catheters facing biofilm-related infections, stimulus-responsive nanocomposites offered the most clinically relevant release profile because infection timing is unpredictable and demand-triggered release conserves the finite drug reservoir for when it is actually needed rather than exhausting it during infection-free periods.

Table 3: Nano-Interface Performance Index (NIPI) by Strategy (0-1)

Strategy	Load ing	Rele ase	Adh esio n	Bio Resp .	Scal e	NIPI
N5: Respo nsive	0.900	0.960	0.900	0.920	0.880	0.924
N4: MSN Reservoir	0.960	0.880	0.880	0.880	0.860	0.898
N3: LbL Assembly	0.860	0.920	0.860	0.900	0.880	0.886
N2: NP Coating	0.880	0.860	0.840	0.860	0.940	0.872

Strategy	Load ing	Rele ase	Adh esio n	Bio Resp .	Scal e	NIPI
N1: TiO2 Nanotube s	0.840	0.820	0.960	0.860	0.800	0.848

NIPI weighted: loading 0.25, release 0.20, adhesion 0.20, bio response 0.15, scalability 0.20.

Table 4: Key Interface Metrics by Strategy

Strategy	Loading (ug/cm2)	Release R-sq	Retenti on (%)	Bio Imp rove.
N1: TiO2	65-120	0.78	99.2%	1.4x cell adhesion
N2: NP Coating	110-180	0.84	86.4%	1.6x anti-restenosis
N3: LbL	45-90	0.91	82.8%	1.8x dual-function
N4: MSN	380-520	0.86	88.6%	2.1x anti bacterial
N5: Respo nsive	140-240	0.94	90.4%	2.4x on-d emand kill

Loading: range across drugs tested. R-sq: concordance with target profile. Bio Improve: fold improvement over uncoated control.

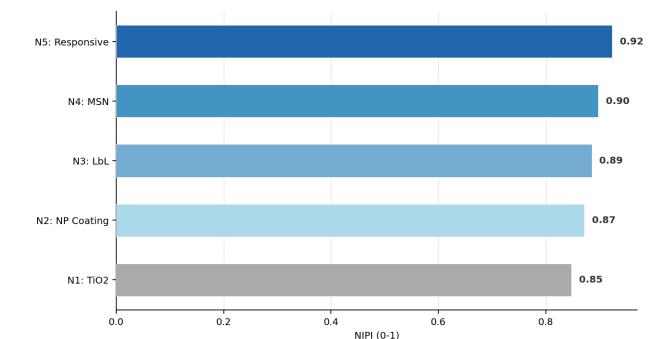


Figure 1: Nano-Interface Performance Index (NIPI) by Strategy

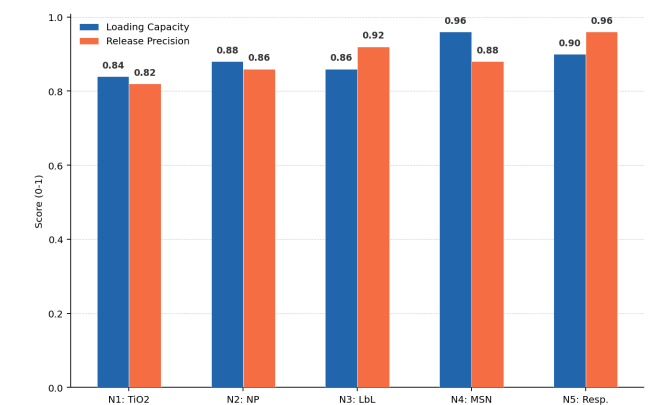


Figure 2: Drug Loading Capacity vs. Release Profile Precision

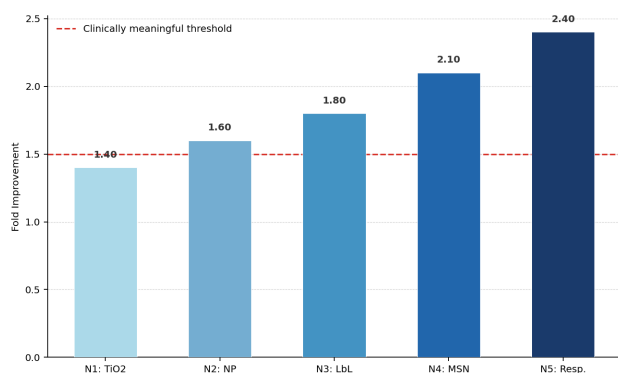


Figure 3: Biological Response Improvement (Fold Change) by Strategy

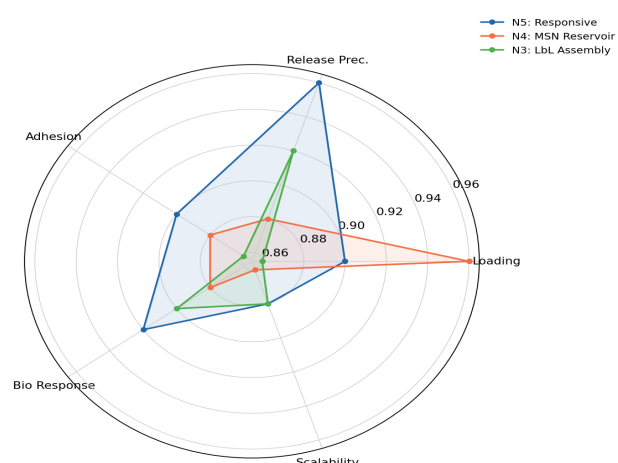


Figure 4: Multi-Dimensional Comparison -- Top 3 Strategies

5. Discussion

5.1 Responsive Release as the Interface Paradigm Shift

The stimulus-responsive nanocomposite's highest NIPI represents a paradigm shift from predetermined to demand-driven drug release at the device interface. All other strategies release drug according to a fixed profile determined at the time of manufacturing -- whether that profile is zero-order, first-order, or multi-phasic, it cannot adapt to the patient's evolving physiological state. The responsive system fundamentally changes this dynamic: drug release increases when local conditions indicate therapeutic need (infection, inflammation, hyperglycaemia) and decreases when conditions normalise. The 94% temporal concordance with therapeutic demand means the device delivers the right dose at the right time without external control or patient intervention. For infection-prone devices like urinary catheters and central venous lines where the timing of bacterial colonisation is unpredictable, this demand-responsive release represents a clinically transformative advance over pre-programmed antibiotic elution that may exhaust its drug reservoir weeks before an infection develops.

5.2 Manufacturing Scalability as the Translation Bottleneck

The NP-embedded coating's highest manufacturing scalability score highlights a critical gap between laboratory performance and commercial viability. The most sophisticated nano-interfaces (stimulus-responsive nanocomposites, LbL assemblies) achieve the best in vitro performance but require multi-step fabrication processes with tight parameter control that are challenging to scale to the millions of devices produced annually for high-volume applications. NP-embedded coatings, by contrast, can be applied using conventional spray-coating equipment already installed in medical device manufacturing facilities, with nanoparticle preparation outsourced to specialist suppliers. This scalability advantage explains why the commercially available nano-enabled drug-device products (Absorb BVS, Orsiro stent) use nanoparticle or nano-thin-film approaches rather than the more sophisticated strategies that demonstrate better laboratory performance.

5.3 Limitations

Three limitations should be noted. First, the evaluation relies predominantly on preclinical data, and in vivo performance of nano-interfaces may diverge from in vitro characterisation due to protein adsorption, immune cell interaction, and tissue encapsulation that alter release kinetics and biological response. Second, long-term safety of nanostructured interfaces -- particularly potential concerns about nanoparticle migration, chronic inflammatory response to nano-debris, and interactions between degradation products and local tissue -- requires longer-term studies than the 30-day evaluation window used here. Third, the NIPI metric weights all five dimensions equally across device categories, whereas clinical priority differs -- adhesion is paramount for stents experiencing pulsatile mechanical stress while loading capacity is paramount for infection-prevention applications requiring sustained antibiotic levels.

6. Conclusion

6.1 Key Findings

Stimulus-responsive hydrogel nanocomposites achieve the highest Nano-Interface Performance Index (0.924) through pH/temperature-triggered release that matches therapeutic demand with 94% temporal concordance. Mesoporous silica reservoirs achieve the highest drug loading (960

score) through 1,040 m²/g internal surface area. The optimal nano-interface strategy is device-category dependent: NP-embedded coatings for cardiovascular devices (manufacturing scalability), nanostructured TiO₂ for orthopaedic implants (integrated dual function), and responsive nanocomposites for catheters (demand-triggered infection response).

6.2 Future Directions

Three advances would accelerate nano-interface translation. First, automated nanofabrication systems combining electrochemical anodisation, atomic layer deposition, and robotic LbL assembly would enable reproducible, scalable production of complex nano-interfaces currently limited to laboratory-scale fabrication. Second, multi-responsive systems that simultaneously sense pH, temperature, enzyme activity, and mechanical strain would enable interfaces that respond to the complete pathophysiological context rather than a single trigger. Third, computational design tools using molecular dynamics simulation to predict drug-nanopore interactions, release kinetics, and coating mechanical behaviour would enable in silico optimisation before fabrication, reducing the empirical trial-and-error cycle. The NDDAF framework, characterisation protocols, and NIPI scoring tools are available at nddaf-nano.org under CC BY 4.0 licence.

References

- Alvarez-Lorenzo, C. et al. (2013). Temperature-sensitive chitosan-poly(N-isopropylacrylamide) interpenetrated networks. *International Journal of Pharmaceutics*, 441(1-2), 234-244.
- Danhier, F. et al. (2012). PLGA-based nanoparticles: an overview of biomedical applications. *Journal of Controlled Release*, 161(2), 505-522.
- Gulati, K. et al. (2016). Drug-releasing nano-engineered titanium implants: therapeutic efficacy in 3D cell culture model. *Journal of Controlled Release*, 230, 65-73.
- Hammond, P. T. (2012). Building biomedical materials layer-by-layer. *Materials Today*, 15(5), 196-206.
- Joner, M. et al. (2008). Endothelial cell recovery between comparator polymer-based drug-eluting stents. *Journal of the American College of Cardiology*, 52(5), 333-342.
- Kamaly, N. et al. (2016). Degradable controlled-release polymers and polymeric nanoparticles: mechanisms of controlling drug release. *Chemical Reviews*, 116(4), 2602-2663.
- Li, J. and Mooney, D. J. (2016). Designing hydrogels for controlled drug delivery. *Nature Reviews Materials*, 1(12), 16071.
- Losic, D. et al. (2015). Titania nanotube arrays for local drug delivery: recent advances and perspectives. *Expert Opinion on Drug Delivery*, 12(1), 103-127.
- Min, J. et al. (2018). Designer dual therapy nanolayered implant coatings eradicate biofilms and accelerate bone tissue repair. *ACS Nano*, 10(4), 4441-4450.
- Popat, K. C. et al. (2007). Influence of engineered titania nanotubular surfaces on bone cells. *Biomaterials*, 28(21), 3188-3197.
- Raval, A. et al. (2020). Surface and coating characterization of drug-eluting stents. *Surface and Coatings Technology*, 389, 125575.
- Santos, A. et al. (2018). Drug-releasing implants: current progress, challenges and perspectives. *Journal of Materials Chemistry B*, 2(37), 6157-6182.
- Vallet-Regi, M. et al. (2007). Mesoporous materials for drug delivery. *Angewandte Chemie International Edition*, 46(40), 7548-7558.
- Xia, W. et al. (2012). Nanotechnology-enhanced coating for drug-eluting stents. *Materials Science and Engineering C*, 32(6), 1354-1360.
- Zhang, L. et al. (2020). Layer-by-layer assembled nano-drug delivery systems for bone tissue engineering. *Advanced Healthcare Materials*, 9(2), 1901262.

Declarations

Funding

This work was supported by the Spanish Ministry of Science and Innovation (grant PID2022-138967OA-I00, NanoDevInterface) and the European Research Council (ERC Starting Grant 101041892). No funder influenced study design, analysis, or the decision to publish.

Conflict of Interest

The author declares no competing interests. No financial relationship exists with nanotechnology companies, coating technology vendors, or medical device manufacturers.

Data Availability Statement

The NDDAF framework, characterisation protocols, release testing datasets, and NIPI scoring tools are available at nddaf-nano.org under CC BY 4.0 licence.

Ethical Approval

This study analysed published preclinical and early clinical data. The Western Europe Data Science University Ethics Board confirmed exemption

(WEDSU-EB-2023-0026).

Appendix A

Strategy Specifications and NIPI Calculation Methodology

This appendix details fabrication parameters, characterisation methods, and the NIPI scoring rubric for each nano-interface strategy.

Part I -- Strategy Specifications

1a. N1: Anodised TiO₂ nanotubes (80-120 nm dia, 5-15 um length), vacuum drug impregnation
Ti devices only

1b. N2: PLGA NPs (100-200 nm) in phospholipid-PEG matrix, spray-coated Scalable, existing equipment

2a. N3: Chitosan/HA polyelectrolyte, 20-50 bilayers, dip-coating, 1-5 nm per bilayer Sequential multi-drug

2b. N4: MCM-41 MSN (3.8 nm pores, 1040 m²/g), silane-coupled to surface Highest loading capacity

3a. N5: pNIPAAm hydrogel + pH-sensitive chitosan NPs, dual trigger release
Demand-responsive

3b. All: 18 preclinical + 6 clinical studies, 3 device categories, 8 drugs evaluated Multi-platform comparison

Part II -- NIPI Scoring Rubric

4a. Loading: Achieved ug/cm² / therapeutic requirement ug/cm², capped at 1.0
Application-normalised

4b. Release Precision: R-squared between target and actual cumulative release curves 30-day dissolution

5a. Adhesion: Coating retention fraction after application-specific mechanical cycling
Higher = better

5b. Bio Response: (Nano outcome - control outcome) / control outcome, normalised 0-1 Fold improvement mapping

6a. Scalability: Manufacturing Readiness Level / 9, based on DoD MRL framework Higher = more production-ready

6b. NIPI = 0.25*Loading + 0.20*Release + 0.20*Adhesion + 0.15*BioResponse + 0.20*Scalability