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Stress Testing Methods for Implantable Electronic Devices Under Simulated Physiological Environment Conditions

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Abstract

The article explores stress testing methods used to evaluate the reliability and durability of implantable electronic devices under simulated physiological environment conditions. Implantable bioelectronic systems operate in complex biological environments where moisture ingress, mechanical strain, chemical reactions, and biological responses can progressively degrade device performance and ultimately cause failure. The article used a comparative analysis of recent experimental studies on implant reliability, encapsulation technologies, accelerated aging tests, and lifetime modeling methods reported in contemporary bioelectronics literature. Particular attention was given to in-vitro accelerated aging experiments, thin-film encapsulation barriers, electrical monitoring techniques for insulation failure, and statistical lifetime analysis methods such as Weibull modeling. The main results are that accelerated aging in physiological solutions combined with continuous electrical monitoring provides a reliable method for determining time-to-failure of implantable devices, while modern encapsulation technologies—such as thin-film multilayer barriers, silicon carbide coatings, and atomic layer deposition—significantly influence device longevity. The results also show that failure mechanisms typically arise from coupled electrical, mechanical, chemical, and biological degradation processes rather than from a single dominant factor. The article will be useful to researchers and engineers working in bioelectronics, neural interface design, and biomedical device reliability, as well as to specialists involved in the development, testing, and regulatory evaluation of implantable medical technologies.

Keywords: *Implantable Electronics; Accelerated Lifetime Testing; Thin-Film Encapsulation; Neural Implant Reliability; Physiological Environment Simulation.*

INTRODUCTION

Implantable electronic devices operate in one of the most demanding engineering environments: a warm, wet, ion-rich medium that is mechanically active and biologically reactive, continuously challenging electrical insulation, interfacial adhesion, structural integrity, and functional stability. Unlike conventional electronics, implantable systems cannot be evaluated solely by their nominal performance at fabrication. Their practical value depends on whether function is maintained over clinically meaningful periods while the device is exposed to saline fluids, voltage bias, cyclic strain, corrosion, protein adsorption, tissue responses, and packaging defects that may remain latent until operation in vivo begins [3], [5], [14]. For that reason, stress testing is not a peripheral development step in this field. It is one of the main ways designers estimate lifetime, compare materials and architectures, identify dominant failure routes, and generate evidence for verification, validation, and regulatory confidence [12], [13].

At the same time, the literature remains methodologically fragmented. Studies apply different media, temperatures, voltages, monitoring strategies, and failure criteria; some examine isolated materials, others test simplified structures, and only a minority examine full device-level behavior [2], [7]–[11]. As a result, the field contains a large amount of experimental data, but there is still no consistent way to interpret what a given stress test actually predicts. A coating that appears stable in a material study may fail once real edges, feedthroughs, or mechanically strained interfaces are present. Thermal acceleration can also shorten lifetime while changing the dominant failure pathway compared with operation at body temperature [2], [8]. The central issue is therefore not only how to accelerate degradation, but how to select a stress model that reflects the failure mode governing device lifetime.

This paper examines stress-testing methods reported in experimental studies, reviews, translational research, and regulatory sources, and compares them in terms of the

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types of vulnerability they reveal in implantable electronic systems. Rather than treating saline immersion, thermal aging, electrical acceleration, permeation sensing, adhesion testing, and long-term device validation as interchangeable measures of "durability," the paper interprets them as selective probes of specific degradation logic. In doing so, it shifts the discussion from the search for a single best accelerated-aging protocol toward a mechanism-oriented and architecture-aware framework for stress testing. Failures in implanted electronic systems usually do not develop uniformly. In many studies the first signs of deterioration appear near structural transitions in the package. Electrode openings and trace edges are typical locations. For this reason, device-level tests are often used to identify where the barrier begins to lose its protective function.

METHODS AND MATERIALS

This study used a comparative literature-review method.It analyzed 15 uploaded sources on stress testing of implantable electronic devices under simulated physiological conditions, among them experimental papers, review articles, and FDA regulatory documents. The methods described in these sources were saline/buffer immersion in Ringer solution or PBS, thermal accelerated aging, electrical accelerated aging under voltage bias, electrochemical impedance spectroscopy (EIS), continuous leakage/voltage monitoring, WVTR and permeation assessment, peel/adhesion testing, microscopy, and wireless real-time barrier monitoring.

Cho et al. reported a fully bioresorbable hybrid opto-electronic neural implant capable of simultaneous electrophysiological recording and optogenetic stimulation [1]. Insulation lifetime in neural implant test structures was examined by Guljakow and Lang using in-vitro experiments with thermal acceleration in physiological solution [2]. Mariello et al. presented a review of encapsulation materials, barrier technologies, and characterization methods developed for flexible bioelectronic implants [3]. Mariello et al. then addressed a different aspect by presenting a wireless, battery-free platform for real-time monitoring of water permeation across thin-film encapsulation [4]. Mariello's later perspective article focused on reliability and stability in bioelectronic medicine and organized implant failures into electrical, mechanical, chemical, and biological classes [5]. Mehra et al. reported final MOMENTUM 3 outcomes for the fully magnetically levitated HeartMate 3 device, which served here as a benchmark for long-term implanted electromechanical reliability [6]. Nanbakhsh et al. investigated the longevity and inherent hermeticity of silicon integrated circuits through accelerated aging and implantation experiments that compared bare-die devices with PDMS-coated ones [7]. Nguyen et al., in contrast, studied amorphous silicon carbide encapsulation under voltage-driven accelerated aging and analyzed the resulting degradation and failure transitions [8].

Novák et al. described a low-cost, prototype-friendly encapsulation route based on epoxy overmolding, hermetic feedthroughs, and biocompatibility testing for implantable electronics [10]. Pak et al. compared thin-film coating systems for LCP-based flexible bioelectronic implants using lifetime-estimation methodologies and barrier-performance testing [11]. The FDA design-control guidance was included because it framed reliability work in terms of verification, validation, risk analysis, and traceable development controls [12]. The FDA PMA documentation for the HeartMate 3 LVAD was included as a real-device validation source showing how reliability claims are supported in regulatory practice [13]. Yogev et al. provided a broader engineering review of implantable sensors, linking physiological stress exposure to practical design and translation challenges [14]. Zhang et al. used double-electrode electrochemical experiments to clarify processes occurring at PEDOT-coated neural electrode arrays, which made the source useful for electrode-level degradation and electrochemical response mechanisms [15].

Several limitations remain in the current literature base. The reviewed studies do not use a common failure definition, which makes cross-study comparison difficult [2], [8], [9], [11]. They also differ in whether they test isolated materials, test structures, partially assembled devices, or functional implants, so reported lifetimes are not directly interchangeable [1], [2], [7]–[11]. In addition, combined-stress protocols remain less developed than single-stressor protocols, even though the evidence strongly suggests that real implant degradation is coupled rather than isolated [3], [5], [14]. These limitations do not weaken the main conclusion of the article. On the contrary, they reveal where the field is still methodologically immature.

RESULTS

The analyzed sources showed that stress testing of implantable electronic devices was performed in several simulated physiological environments rather than through a single standardized protocol. The most common media were Ringer solution, PBS, and buffered saline systems operated at physiological temperature or under elevated-temperature acceleration. Across the reviewed studies, the main test structures included polyimide-encapsulated interdigitated conductors, a-SiC-coated interdigitated electrodes, Au interdigitated comb structures on LCP substrates, polymer microelectrode arrays with thin-film barriers, partially PDMS-coated silicon ICs, epoxy-encapsulated implantable circuit boards, and fully bioresorbable opto-electronic neural implants [1], [2], [7]–[11].

Stress-testing studies used a variety of readout methods. Some relied on electrochemical impedance spectroscopy, sorption-derived WVTR estimation, peel testing, and optical or electron microscopy, whereas others used continuous electrical monitoring, progressive-stress voltage stepping,

or wireless in-situ permeation sensing [2], [4], [8], [11]. Distinctive approaches included the continuous voltage-drop method used by Guljakow and Lang instead of periodic EIS, the voltage-driven accelerated-aging model for a-SiC devices described by Nguyen et al., and the wireless battery-free monitoring platform for real-time water permeation reported in the Mariello-related studies [2], [4], [8]. Table 1 summarizes the diversity of experimental configurations used to evaluate the reliability of implantable electronic devices under simulated physiological conditions.

Table 1. Comparative map of simulated physiological test environments, device structures, and readouts across the reviewed studies

Device / Test Structure	Medium	Stress Type	Main Readout	Failure Criterion / Key Output
Polyimide interdigitated conductors	Ringer's solution	Thermal accelerated aging (37 °C vs 57 °C)	Continuous voltage monitoring (voltage-drop method)	Lifetime distribution, median lifetime (363 vs 138 days), Weibull scale and shape parameters
a-SiC IDEs (amorphous silicon carbide)	Phosphate-buffered saline (PBS)	Electrical accelerated aging with stepped voltage bias	Leakage-current monitoring and electrical characterization	Onset of leakage excursions (~+2 V / −3 V), breakdown voltage (~2.5–3.3 V), time-to-failure distributions
LCP IDC structures (liquid crystal polymer interdigitated capacitors)	PBS at elevated temperature	Combined electrical bias and thermal aging	Electrical impedance / leakage monitoring	Long-term functionality under bias (up to ~28 months), stability of encapsulation layers
Polymer microelectrode arrays with ALD/ALI encapsulation	Buffered saline	Long-term immersion with electrical characterization	EIS and microscopic failure analysis	Barrier degradation, delamination, insulation failure at coating defects
PDMS-coated silicon integrated circuits	Saline / physiological solution	Long-term immersion testing	Electrical functionality monitoring and microscopy	Water permeation through encapsulation and subsequent electronic malfunction
Epoxy-overmolded prototype electronics	Physiological saline	Long-duration immersion testing	Functional electronic testing and visual inspection	Encapsulation integrity and electrical functionality over time
Bioresorbable opto-electronic implant	In vivo physiological environment	Long-term implantation and natural degradation	Wireless optical/ electrical monitoring and imaging	Controlled biodegradation and functional lifetime of the implant

As presented in Table 1, the reviewed studies employed several representative device structures, including polyimide interdigitated conductors, amorphous silicon carbide (a-SiC) IDEs, liquid crystal polymer (LCP) interdigitated capacitors, polymer microelectrode arrays, PDMS-coated silicon integrated circuits, epoxy-encapsulated prototype electronics, and bioresorbable opto-electronic implants. These systems were exposed to physiological media such as Ringer's solution, phosphate-buffered saline (PBS), buffered saline environments, or in vivo conditions. Stress protocols differed substantially among the studies summarized in Table 1. Reported approaches included thermal accelerated aging, voltage-driven electrical stressing, combined thermal–electrical loading, and long-term exposure through implantation or immersion.

Diagnostic methods also varied. Electrical monitoring techniques such as continuous voltage tracking, impedance spectroscopy, and leakage-current measurements were commonly used. Materials-oriented measurements included WVTR analysis, peel-strength testing, microscopy, and in some cases wireless permeation sensing. The experiments produced several types of outputs, including device lifetime or time-to-failure distributions, onset of leakage or breakdown behavior, degradation of encapsulation barriers, water permeation through protective layers, and controlled biodegradation of transient implants. Table 1 summarizes the device structures, environmental media, and measurement techniques used in these stress tests and the associated failure mechanisms observed under simulated physiological conditions.

Figure 1 shows how the clearest thermal accelerated-aging dataset was reported for polyimide-based neural implant test structures immersed in Ringer solution at 37 °C and 57 °C.

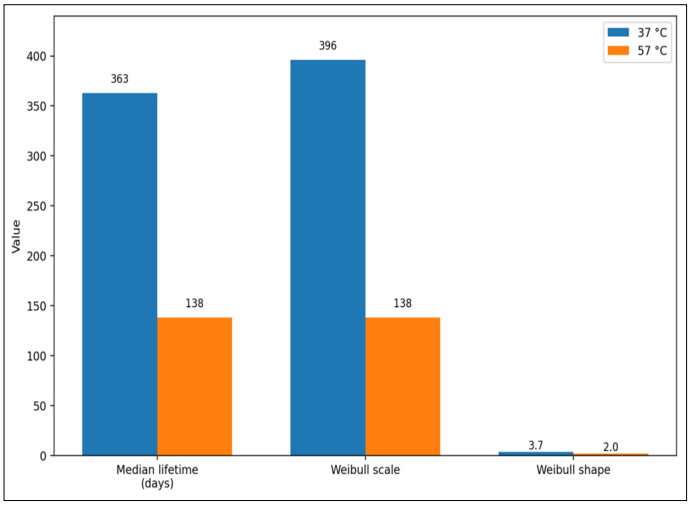

Figure 1. Thermal accelerated-aging results for polyimide neural implant test structures at 37 °C and 57 °C based on the study by Guljakow and Lang

Figure 1 shows that median lifetime decreased from 363 days at 37 °C to 138 days at 57 °C, while the Weibull scale and shape parameters changed from 396 and 3.7 to 138 and 2.0, respectively [2]. The experiment continued for 458 days at 37 °C and 423 days at 57 °C, and several samples remained intact when the tests ended, producing right-censored lifetime data [2]. The measured acceleration factor was about 2.65 rather than the fourfold reduction predicted by the conventional Van't Hoff assumption for a 20 °C temperature increase. The corresponding reaction-rate constant was estimated at approximately 1.47 [2]. These data established that thermal acceleration shortened lifetime substantially but not according to the commonly assumed proportional model.

Electrical accelerated aging produced a different quantitative profile. Figure 2 illustrates the shift from capacitive behavior at low voltage to Faradaic leakage and eventual breakdown as voltage stress increases.

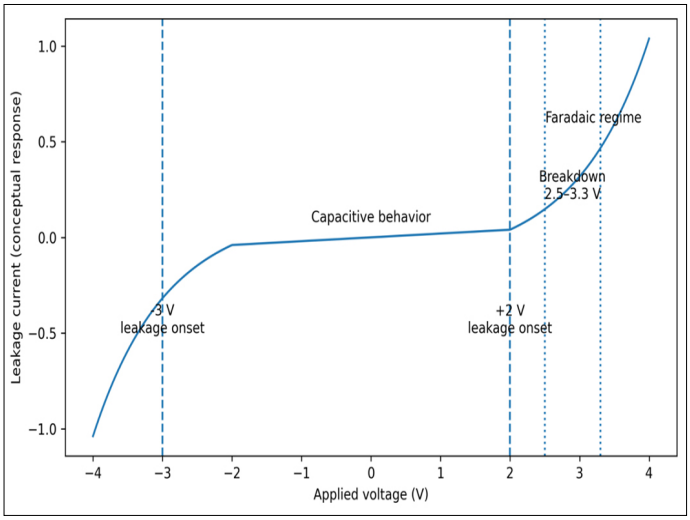

Figure 2. Electrical accelerated aging of a-SiC encapsulation: leakage transition and breakdown behavior under stepped voltage stress based on the data by Nguyen et al.

Figure 2 shows leakage behavior for IDEs tested in PBS at 37 °C. Large excursions appeared near +2 V and −3 V during progressive voltage stressing [8]. Failure corresponded to a shift from capacitive to Faradaic response rather than crossing a fixed leakage threshold. The breakdown region lay roughly between 2.5 and 3.3 V with voltage steps of about 0.1 V. Geometric mean failure times were 1588.0 s, 2323.4 s, and 6134.9 s for step durations of 1, 2, and 5 min, respectively [8].

Longer-duration barrier-performance results were reported for LCP-based systems. In PBS at 60 °C under a continuous 14 V DC bias, LCP-LCP encapsulated IDC structures remained functional for up to 28 months, while TFE1-silicone devices maintained functionality for at least 16 months; by contrast, TFE2-silicone samples under 14 V bias failed around month 4 [11]. Failure in that study was defined as a deviation of more than 10% in impedance magnitude at 0.1 Hz relative to the baseline value [11]. Using this criterion, devices remained functional for long periods, although the observed stability depended on both coating architecture and the applied stress conditions.

In addition to endpoint failure, several studies assessed encapsulation through barrier-related measurements. Ultrahigh barrier systems for flexible implants require measurement sensitivity below about 10^-6–10^-7 g m^-2 day^-1, and moisture ingress should ideally be monitored with in-situ techniques rather than inferred only after endpoint failure [3]. In the encapsulation review, moisture ingress was discussed as a parameter that should be tracked with in-situ techniques instead of being inferred only after endpoint failure [3]. Separate experiments have monitored water permeation through thin-film encapsulation in real time [4]. A reported implementation uses a wireless, battery-free platform based on magnesium corrosion and backscatter communication to detect moisture penetration through thin-film encapsulation layers [4].

Barrier comparisons also showed that low WVTR alone did not guarantee long lifetime. In the LCP coating study, WVTR values at 60 °C/60% RH were 202.05 mg/m^2 day for bare LCP, 2.87 mg/m^2 day for LCP-TFE1, and 2.23 mg/m^2 day for LCP-TFE2, but bending sharply increased WVTR for both thin-film systems, especially TFE1, from 2.87 to 68.61 mg/m^2 day [11]. The same study explicitly concluded that adhesion to the substrate, not WVTR alone, played a key role in maintaining lifetime stability [11]. T-peel results also differentiated the stacks, with LCP-TFE1-silicone showing an 8 N peel force, while LCP-TFE2-silicone showed only 0.1 N [11].

Additional results from other sources supported the same pattern. Nanbakhsh et al. found that silicon ICs maintained stable electrical performance after one year of accelerated in vitro and in vivo testing, even under direct exposure to physiological fluid [7]. At the same time, material analysis showed degradation in exposed bare-die regions. The PDMS-coated regions were affected much less. The authors

therefore argued that, together with the intrinsic hermeticity of the die, PDMS coating could support operation over much longer periods For prototype-scale electronics, Novák et al. reported that epoxy overmolding with hermetic feedthroughs improved resistance to liquid ingress compared with simple PDMS or epoxy potting, while the encapsulant Loctite EA M-31 CL had a dielectric breakdown voltage of 19.7 kV/mm and the encapsulated structure was tested up to 333 V/m [10].

Across the reviewed sources, the same classes of degradation recurred. Figure 3 shows the broadest classification dividing failures into electrical, mechanical, chemical, and biological categories, including insulation breakdown, electrode corrosion, fracture, delamination, chemical attack by ions and reactive species, fibrotic encapsulation, and biofouling [5].

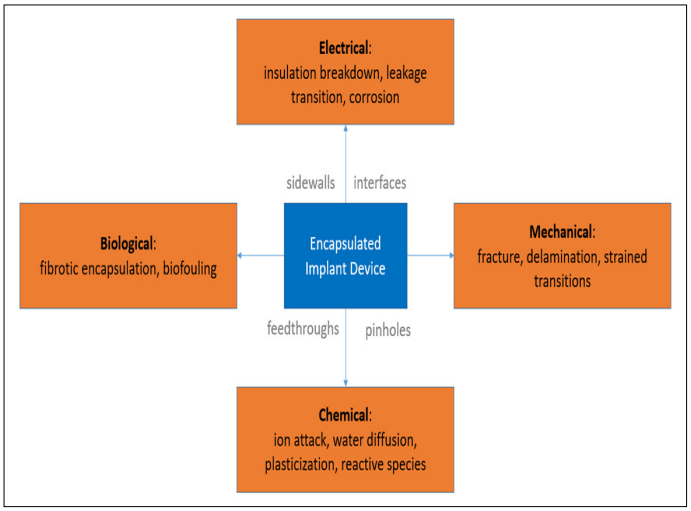

Figure 3. Recurring degradation routes and structurally vulnerable regions identified across the reviewed studies (the author's illustration)

At the center of Figure 3 is the encapsulated implant device, which contains protective layers and interfaces intended to isolate electronic components from the physiological environment. Surrounding the device are four major classes of degradation mechanisms: electrical, mechanical, chemical, and biological. Electrical degradation includes insulation breakdown, leakage transitions, and corrosion processes that can disrupt circuit functionality. Mechanical degradation involves fracture, delamination of layers, and strain concentrations at material transitions. Chemical degradation arises from ion attack, water diffusion through encapsulation layers, polymer plasticization, and reactions with chemically active species in the physiological environment. Biological degradation includes fibrotic encapsulation and biofouling associated with tissue responses and protein deposition. In practice, these effects tend to appear first at vulnerable regions of the device, including sidewalls, material interfaces, feedthroughs, and microscopic pinholes in the encapsulation barrier, where local exposure to the environment or mechanical loading can undermine protection. The device-focused studies reviewed by Mariello fit this same four-part classification [5].

Moisture ingress and interfacial degradation appear repeatedly in the reviewed literature. Mariello identified several processes associated with encapsulation failure, including water diffusion, swelling, plasticization, interfacial transport, and the formation of water clusters within barrier layers [3]. Niemiec et al. similarly reported that sidewall regions remain a major vulnerability in thin-film polymer microelectrode arrays. Their experiments showed that 3D-ALI deposition improved protection of the sidewall region compared with conventional ALD, although this modification did not produce a measurable increase in overall device lifetime [9]. WVTR in that study varied with defect size over roughly three orders of magnitude, from about 8 × 10^-3 to 8 × 10^-6 g/m^2/day [9]. Such variation is relevant for long-term water sorption and device stability.

In amorphous silicon carbide encapsulation, failure was associated mainly with processing-related defects rather than with uniform degradation of the barrier. Reported defect sites included particulate contamination, pinhole-type openings, voids at metallization steps, trace-edge irregularities, and gas-bubble-related damage that ultimately led to dissolution of the underlying Au/Ti metallization [8]. Guljakow and Lang observed a different failure pattern in polyimide-encapsulated interdigitated conductors: insulation breakdown produced a sudden increase in leakage current, and the temperature-dependent change in the Weibull shape parameter suggested that elevated temperature altered the dominant failure mechanism rather than simply accelerating the same process [2]. In the bioresorbable opto-electronic implant, the results instead defined a controlled degradation window: simultaneous optical stimulation and electrophysiological recording was maintained for about 2 weeks, while complete biodegradation occurred within 8 weeks; the device geometry included a 20 µm PLGA substrate, 280 × 280 µm^2 grid electrodes, and a 105 µm optical fiber core [1].

Stress testing in the analyzed studies was carried out under several types of simulated physiological conditions. Many experiments relied on immersion in saline or buffered media while accelerating degradation either by elevated temperature or by electrical bias. Device behavior during testing was commonly followed through electrical measurements, including impedance changes or the appearance of leakage currents. Some recent work also used diagnostic methods that track moisture penetration through the encapsulation barrier in real time. The experiments produced several quantitative indicators of reliability. Reported values included device lifetime, statistical time-to-failure distributions, breakdown voltage, WVTR measurements, and adhesion strength of protective layers. Observed degradation mechanisms were most often related to moisture ingress, instability at material interfaces, dielectric failure associated with defects, corrosion processes, or mechanically stressed regions of the device.

DISCUSSION

The reviewed sources suggest that the central problem in stress testing implantable electronic devices is not simply reproducing "physiological conditions," but deciding which failure logic is being simulated. Saline immersion, elevated temperature, voltage bias, mechanical deformation, and long-term implantation do not represent equivalent versions of the same hazard. Rather, they activate different degradation pathways and expose different weak points in the device [2]–[5], [8]–[11], [14]. This means that stress testing in this field should not be understood as a search for one universal accelerated-aging protocol. Stress testing should be chosen with the likely failure site of the device in mind. Bulk encapsulation properties by themselves do not account for implant reliability.

In the studies reviewed here, the barrier material was often not the part that failed first. Degradation was more often found at interfaces, sidewalls, feedthroughs, metallization steps, and similar small geometric irregularities in the structure [8]–[11]. In many engineering discussions encapsulation is approached mainly as a materials problem, where a low-permeability coating is deposited and reliability is assumed to follow from the barrier chemistry. Niemiec et al. reported that 3D-ALI barriers provided better protection at device sidewalls than conventional ALD deposition.. However, the modification did not produce a statistically significant increase in device lifetime in their experiments [9]. In a different study, Pak et al. examined thin-film coatings for LCP-based implants and observed that coatings with favorable water-barrier properties could still fail when adhesion to the substrate or interfacial stability was poor [11]. Novák et al. identified cable feedthroughs rather than the epoxy bulk as the main ingress route [10], while Nguyen et al. localized electrical failure around defects, step coverage irregularities, and exposed metallization [8]. Taken together, these sources support a stronger interpretation: the lifetime of an implant is often governed less by the average quality of the encapsulant than by the worst local transition in the package architecture.

This has a direct consequence for how stress-testing results should be interpreted. When a coating is described as "stable," that statement may only apply to the coating as a film, not to the device as an assembled system. In many implantable systems, failures appear at structural transitions. The bulk encapsulation material is not always where degradation begins. Reported failures frequently occur where the barrier layer is interrupted — for example near electrode openings or along trace edges. Interfaces connected to flexible substrates or wires are also commonly involved [8]–[11]. Because of this, experiments that examine complete device assemblies tend to provide more realistic lifetime information. Tests limited to isolated materials often miss these architectural weak points. Material characterization therefore remains important, but it can give an overly optimistic impression of reliability if the architectural features that create real failure pathways during operation are not included in the test structure.

Thermal acceleration also has limitations as a predictive shortcut. Guljakow and Lang provide a useful illustration of this point. In their experiments, increasing temperature from 37 °C to 57 °C shortened device lifetime, yet the reduction did not match the commonly cited expectation that a 20 °C increase should lead to approximately a fourfold acceleration [2]. In addition, the Weibull shape parameter varied with temperature, indicating that higher temperature did not simply accelerate the same failure mechanism but altered the statistical pattern of failure itself [2]. This observation has methodological implications. Although thermal aging shortens experimental duration, it does not represent a neutral compression of real time. Elevated temperature can influence swelling behavior, diffusion processes, interfacial stresses, electrochemical reactions, and polymer degradation in different ways and to different degrees [2]–[5]. Consequently, thermal acceleration is more appropriately interpreted as a screening or comparative tool rather than as a direct predictor of aging under physiological conditions. In other words, faster failure at higher temperature does not guarantee that the same mechanism would dominate at body temperature.

The contrast between thermal aging and electrical accelerated aging sharpens this point further. Nguyen et al. did not simply accelerate time; they accelerated a specific failure route by applying electrical stress and tracking the shift from capacitive to Faradaic behavior [8]. In the experiments reported by Nguyen et al., the electrical response of the encapsulated structures changes before complete device failure occurs. As voltage stress increases, the behavior of the electrodes shifts from capacitive to Faradaic leakage, indicating that the insulating barrier is beginning to break down [8]. This transition appears before catastrophic leakage or loss of device function. A fixed threshold is easy to apply, but a mechanistic transition often corresponds more closely to the processes occurring inside the device.

Implantable devices rarely fail as a single sudden event. Electrical breakdown is often preceded by slower changes inside the protective layers. Moisture may enter the barrier, polymer films can swell, and interfaces between materials may begin to separate while the electrical behavior of the device still appears normal [3]–[5], [8]. Because of this, periodic impedance measurements or post-mortem examination usually reveal only the stage at which insulation failure has already occurred. Techniques that record device behavior continuously or detect electrical transitions can reveal these earlier stages of degradation and show whether deterioration develops progressively during aging or appears once a defect becomes electrically active.

Another implication of the reviewed sources is that "simulated physiological environment" should not be

treated as synonymous with saline immersion at 37 °C. That setup captures ionic exposure, but real implants face a more complex load profile that can include electric fields, micromotion, repeated bending, interfacial shear, biofouling, tissue response, and in some applications flowing blood or controlled biodegradation [1], [5], [6], [14]. The problem is not that saline immersion is wrong; it is that it is incomplete. For some device classes it may be sufficient as a first-pass screen, but for others it misses the dominant cause of failure. The bioresorbable neural implant in Cho et al. illustrates this clearly: there the relevant question is not how to prevent degradation indefinitely, but how to maintain function for a pre-defined operational window before controlled resorption [1]. The HeartMate 3 literature makes the same point from the opposite direction: long-term implant reliability in circulatory devices cannot be reduced to barrier survival because hemocompatibility, thrombosis, and mechanically mediated blood damage become part of the failure landscape [6]. Thus, the proper physiological simulation depends on what "success" means for the specific implant.

This is why the reviewed evidence argues against a single hierarchy in which one stress-testing method is simply "better" than the others. Raising temperature is a convenient way to shorten a test, but the failure mode seen under those conditions may no longer match the one that develops near body temperature [2]. Electrical stressing is used for a different reason: it more readily brings out dielectric failure and defect-driven breakdown in the encapsulation stack [8]. Some techniques do not aim at final failure at all. Real-time permeation monitoring is useful much earlier, when water first begins to pass through the barrier [5]. Peel and adhesion tests are also informative, because a coating may show acceptable WVTR values and still perform poorly once the interface itself starts to weaken [11]. Tests on assembled prototypes add yet another layer, since they expose practical weak points in the package, especially at feedthroughs and related transitions that do not exist in simplified thin-film specimens [10]. For that reason, reliability is usually judged from several kinds of tests taken together, not from one number obtained by a single protocol.

The same point helps with the 3D-ALI result. Better sidewall protection did not automatically produce longer overall lifetime [9]. In the study using 3D-ALI barriers, enhanced protection at sidewalls did not translate into a clear extension of overall device lifespan [9]. When one degradation mechanism is reduced, the limiting factor often shifts to another part of the structure. In implant packages this typically occurs at interfaces, feedthroughs, or local defects where protective layers are interrupted. Evidence from several studies shows that blocking one ingress route does not eliminate failure but instead redirects it toward the next weakest transition in the device architecture [8]–[11]. In that sense, stress testing should not only estimate lifetime; it should help identify which bottleneck currently governs lifetime.

The uploaded regulatory and translational sources reinforce this interpretation. The FDA design-control guidance emphasizes verification, validation, risk analysis, and worst-case thinking rather than reliance on a single performance test [12]. Read in light of the technical studies reviewed here, that framework implies that stress testing for implantable electronics should be built around architecture-specific risk hypotheses: where moisture is most likely to enter, which interface is most likely to debond, which voltage condition is most likely to trigger electrochemical failure, and which mechanical motion is most likely to crack the barrier [8]–[12]. A stress-testing method becomes valuable when it is linked to such a hypothesis, rather than simply accelerating failure.

Overall, the predictive value of stress testing depends less on how aggressively the device is aged than on how accurately the test reproduces the governing failure pathway of the device. The reviewed literature consistently shows that implant reliability is determined at vulnerable transitions—interfaces, openings, edges, feedthroughs, strained thin films, and defect sites—where moisture, charge, and mechanical stress meet [8]–[11]. A useful stress-testing framework should therefore be mechanism-oriented, architecture-aware, and multi-method. Not all harsh tests are informative, and not all physiologically realistic tests are discriminating. The most valuable ones are those that reveal, as early and as clearly as possible, where the package stops behaving like a package and starts behaving like a failure site.

CONCLUSION

Stress testing of implantable electronic devices cannot be reduced to one universal accelerated-aging recipe. The reviewed literature shows that different test methods activate different degradation pathways, expose different structural weaknesses, and answer different reliability questions. Saline immersion, elevated temperature, electrical bias, barrier-permeation monitoring, adhesion testing, and long-term device validation should therefore not be treated as competing substitutes, but as complementary tools whose value depends on how well they reproduce the governing failure pathway of a given implant [2]–[5], [8]–[14]. What determines how informative a stress test will be is not only the severity of the applied conditions. In many cases, the decisive factor is whether the test actually stresses the structural feature that limits the operating life of the device.

Evidence from the reviewed studies indicates that reliability is frequently governed by localized structural transitions rather than by the average properties of the encapsulating material. Reported degradation repeatedly appeared at device edges, feedthroughs, interfaces between layers, electrode openings, metallization steps, and similar geometric irregularities where protective barriers are interrupted [8]–[11]. This means that material-level barrier metrics remain necessary but are not sufficient on their own. A coating that performs

well as an isolated film may still fail in practical use once real package features are introduced. For that reason, device-level stress testing is often more informative than material-only testing when the purpose is to estimate clinical or preclinical service life.

The reviewed evidence also shows that the field is moving toward more mechanistic and earlier detection of degradation. Continuous leakage monitoring, progressive-stress voltage protocols, and wireless real-time permeation sensing make it possible to detect functional instability earlier rather than waiting for catastrophic endpoint failure [2], [4], [8]. This development aligns stress testing more closely with reliability engineering, where informative tests often identify the point at which insulation begins to lose its protective function rather than the moment when the entire system fails.

Future research should proceed in several directions. First, the field would benefit from more standardized failure definitions and reporting criteria so that lifetime data from different studies can be compared more meaningfully [2], [8], [9], [11]. Second, more combined-stress protocols are needed, especially those integrating thermal, electrical, mechanical, and chemical stressors, because real implant degradation is coupled rather than isolated [3], [5], [14]. Further work is needed on device-level test structures that reflect actual implant architecture, including edges, openings, feedthroughs, flexible transitions, and other vulnerable regions, rather than on idealized barrier films alone [8]–[11]. Accelerated in vitro studies should also be related more closely to in vivo behavior and translational validation, so that reduced test duration does not come at the cost of relevance to the dominant failure mechanism [2], [7], [13]. More attention is needed to in situ and real-time diagnostic methods capable of tracking moisture ingress, interfacial degradation, and electrochemical transition before catastrophic failure occurs [4], [8].

Overall, an effective stress-testing framework for implantable electronics is not necessarily the most aggressive one, but the one that provides the most useful information. Such a framework should remain linked to failure mechanisms, device architecture, statistical interpretation, and the requirements of verification, validation, and risk-based design control. When stress testing is built in that way, it becomes more than a durability screen: it becomes a method for identifying which physical transition presently governs lifetime, and therefore where engineering effort should be directed next.

REFERENCES

1. Cho, M., Han, J.-K., Suh, J., Kim, J. J., Ryu, J. R., Min, I. S., Sang, M., Lim, S., Kim, T. S., Kim, K., Kang, K., Hwang, K., Kim, K., Hong, E.-B., Nam, M.-H., Kim, J., Song, Y. M., Lee, G. J., Cho, I.-J., & Yu, K. J. (2024). Fully bioresorbable hybrid opto-electronic neural implant system for simultaneous electrophysiological recording and optogenetic stimulation. *Nature Communications, 15*(2000), 1-16. https://doi.org/10.1038/s41467-024-45803-0
2. Guljakow, J., & Lang, W. (2023). Analysis of the lifetime of neural implants using in vitro test structures. *Sensors, 23*(6263), 1-11. https://doi.org/10.3390/s23146263
3. Mariello, M., Kim, K., Wu, K., Lacour, S. P., & Leterrier, Y. (2022). Recent advances in encapsulation of flexible bioelectronic implants: Materials, technologies, and characterization methods. *Advanced Materials, 34*(2201129), 1-39. https://doi.org/10.1002/adma.202201129
4. Mariello, M., Rosenthal, J. D., Cecchetti, F., Gao, M., Skrivervik, A. K., Leterrier, Y., & Lacour, S. P. (2024). Wireless, battery-free, and real-time monitoring of water permeation across thin-film encapsulation. *Nature Communications, 15*(7443), 1-14. https://doi.org/10.1038/s41467-024-51247-3
5. Mariello, M. (2025). Reliability and stability of bioelectronic medicine: A critical and pedagogical perspective. *Bioelectronic Medicine, 11*(16), 1-16. https://doi.org/10.1186/s42234-025-00179-4
6. Mehra, M. R., Goldstein, D. J., Uriel, N., Cleveland, J. C., Yuzefpolskaya, M., Salerno, C., Walsh, M. N., Milano, C. A., Patel, C. B., Ewald, G. A., et al. (2019). A fully magnetically levitated left ventricular assist device — Final report. *New England Journal of Medicine*, *380*(17), 1618–1627. https://doi.org/10.1056/NEJMoa1900486
7. Nanbakhsh, K., Idil, A. S., Lamont, C., Dücső, C., Akgun, Ö. C., Horváth, D., Tóth, K., Meszéna, D., Ulbert, I., Mazza, F., Constandinou, T. G., Serdijn, W., Vanhoestenberghe, A., Donaldson, N., & Giagka, V. (2025). On the longevity and inherent hermeticity of silicon-ICs: Evaluation of bare-die and PDMS-coated ICs after accelerated aging and implantation studies. *Nature Communications, 16*(12), 1-17. https://doi.org/10.1038/s41467-024-55298-4
8. Nguyen, C. K., Geramifard, N., Wu, Y., Bhatt, M., Joshi-Imre, A., Negi, S., & Cogan, S. F. (2025). Electrical characterization and accelerated aging of amorphous silicon carbide implantable encapsulation. *Journal of Neural Engineering, 22*(066040), 1-18 https://doi.org/10.1088/1741-2552/ae2956
9. Niemiec, M., Bayansal, F., Bhosale, T., Suib, S., Biyikli, N., & Kim, K. (2025). Failure behavior of polymer microelectrode arrays encapsulated with conventional ALD and 3D-ALI barriers. *Frontiers in Bioengineering and Biotechnology, 13(*1622927), 1-19. https://doi.org/10.3389/fbioe.2025.1622927
10. Novák, M., Rosina, J., Bendová, H., Kejlová, K., Vlková, A., Rucki, M., Svobodová, L., Gürlich, R., & Hajer, J. (2023). Low-cost and prototype-friendly method for

biocompatible encapsulation of implantable electronics with epoxy overmolding, hermetic feedthroughs and P3HT coating. *Scientific Reports, 13*(1644), 1-16. https://doi.org/10.1038/s41598-023-28699-6

11. Pak, A., Nanbakhsh, K., Hölck, O., Ritasalo, R., Sousa, M., Van Gompel, M., Pahl, B., Wilson, J., Kallmayer, C., & Giagka, V. (2022). Thin film encapsulation for LCP-based flexible bioelectronic implants: Comparison of different coating materials using test methodologies for life-time estimation. *Micromachines, 13*(544), 1-14. https://doi.org/10.3390/mi13040544
12. U.S. Food and Administration. (2015, September 30). Design control guidance for medical device manufacturers. https://www.fda.gov/files/drugs/published/Design-Controls---Devices.pdf
13. U.S. Food and Administration. (2026, March 9). *Premarket approval (PMA): HeartMate 3 left ventricular assist device (P160054/S008)*. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p160054s008
14. Yogev, D., Goldberg, T., Arami, A., Tejman-Yarden, S., Winkler, T. E., & Maoz, B. M. (2023). Current state of the art and future directions for implantable sensors in medical technology: Clinical needs and engineering challenges. *APL Bioengineering, 7*(031506), 1-30. https://doi.org/10.1063/5.0152290
15. Zhang, Y., Chen, Y., Contera, S., & Compton, R. G. (2024). Double electrode experiments reveal the processes occurring at PEDOT-coated neural electrode arrays. *ACS Applied Materials & Interfaces, 16*(22), 29439–29452. https://doi.org/10.1021/acsami.4c05204