

Journal of Electronic Systems and Programming



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THE FIRST INTERNATIONAL CONFERENCE ON BIOMEDICAL
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Special Issue – Part C– July 2026

Journal of Electronic Systems and Programming

Electronic Systems and Programming Center

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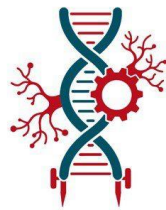
Special Issue – Journal of Electronic Systems and Programming

We are delighted to announce the publication of the second special issue that contains 39 selected papers from **1st International Conference on Biomedical Engineering Science and Technology in Libya**.

The conference aims primarily to establish scientific research bases within academic institutions and research centers in Libya to encourage researchers to present their scientific and research production.

Finally, we thank the conference preparatory committee for choosing JESP to publish the distinguished papers that were presented on the conference.

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**Polymer Melt Differential Electrospinning
Micro/Nanofiber for Biomedical
Applications**

Polymer Melt Differential Electrospinning Micro/Nanofiber for Biomedical Applications

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Abstract

Melt Differential Electrospinning (MDES) is a green and efficient method for fabricating micro/nanofibers. Compared to solution electrospinning, MDES achieves 100% material conversion and eliminates concerns regarding residual solvent toxicity. the integration of multi-field coupled drawing techniques enables the production of ultrafine fibers with tunable diameters ranging from 300 nm to 5 μm . This paper summarizes the primary achievements of our research team in applying MDES technology to the biomedical domain. First, we employed a linear differential nozzle to fabricate fibrous patches. The drug-loaded fibers exhibit unique advantages in controlled drug release, significantly enhancing the final release rate while maintaining stable blood drug concentrations over extended periods (The bioavailability of progesterone fiber patch can reach 1.78 times that of oral administration). Second, we developed an in-situ fiber-forming process based on melt differential electrospinning and established a complete process system from yarn formation to post-processing enhancement. The resulting polylactic acid surgical sutures meet the requirements for 6-0 surgical sutures. After 24 hours of contact with cells, surgical sutures still have a cell survival rate of over 95% and a hemolysis rate of less than 5%. Third, by utilizing an inner-cone differential nozzle, we fabricated artificial dura mater patches, which exhibit favorable mechanical properties compared to native tissues. Fourth, we integrated MDES with Melt Electrowritten (MEW) to produce anisotropic cardiac patches with structural features mimicking natural myocardium. Cell experiments demonstrated that the cellular morphology closely resembled that of native cardiomyocytes. MDES technology provides a safe and controllable platform for fabricating biomedical materials and demonstrates

significant potential for establishing a new paradigm for green manufacturing in biomedicine.

Keywords—Melt Differential Electrospinning, differential nozzle, Micro/Nanofiber, Biomedical Applications

I. INTRODUCTION

The traditional melt electrospinning uses thin tubes as electrospinning nozzles, which are prone to clogging and have low efficiency, seriously affecting the progress of melt electrospinning technology. Inspired by the phenomenon of water splitting in eaves and natural waterfalls, we propose the polymer melt differential electrospinning (MDES) method [1]. Its efficiency is 500 to 1000 times higher than solution electrospinning and about 80 times higher than traditional melt electrospinning [2]. A perforated electrode and an air flow injection device were added between the MDES nozzle and the fiber receiving electrode, constructing a jet stretching system with air flow temperature electrostatic multi-field coupling. The diameter of melt electrospun fibers can be adjusted within the range of 300 nm to 5 μm [3]. Compared to solution electrospinning (ES), MDES directly uses polymer melt without dissolving in organic solvents, avoiding the cost of solvent purchase, recovery, and processing. Only about 10% of the polymer in ES is converted into fibers, while the rest is solvent; The conversion rate of MDES raw materials is nearly 100%, and the spinning efficiency is significantly improved. These undoubtedly provide a solid technical foundation for the application of MDES technology in biomedical fields. This article will introduce our team's research achievements in the field of biomedicine starting from different designs of MDES technology, including drug loaded fiber

transdermal patches, surgical sutures, dura mater patches, labrum stents, and cardiac patches.

II. APPLICATION OF MDES IN BIOMEDICAL FIELD

A. PSA (pressure-sensitive adhesive) Transdermal Patch: Fabrication and Performance

At present, there are many traditional coating methods used in the preparation of transdermal patches both domestically and internationally. However, due to their poor breathability, short storage time, and difficult release control [4], further development is limited. Fiber based drug loaded transdermal patches were prepared by melt electrospinning technology. The porous fiber layer has excellent breathability and can effectively improve medication comfort. The micro-nano solid dispersion of fiber performance can enhance drug solubility, reduce drug precipitation, and have the characteristics of easy regulation of drug release, which can solve the shortcomings of coating patches. Therefore, it has great potential for applications.

We innovatively prepared tandospirone[5] and progesterone-loaded styrene-isoprene-styrene (SIS) PSA fiber patches using melt electrospinning technology, systematically comparing their performance with conventional coating patches. Simultaneously, we used a linear differential nozzle is used to continuously manufacture fiber patches. Experimental results demonstrated that the fibrous structure effectively suppressed initial drug burst release while enhancing terminal release rate. Pharmacokinetic data revealed that the fiber patches achieved 1.79-fold higher bioavailability compared with oral administration and maintained stable blood drug concentration over extended periods. The developed patches simultaneously exhibited excellent adhesion (> 7 day) and

breathability(only 37.06 Pa), providing both theoretical foundation and technical solutions for novel transdermal drug delivery systems.

B. Polylactic Acid (PLA) Surgical Sutures

Common methods for preparing micro nano fiber yarns include two-component composite spinning and solution electrospinning. Two-component composite spinning is the use of traditional melt spinning technology to simultaneously extrude two incompatible or differently characterized polymers from specially designed composite spinnerets[6]. Form continuous composite filaments with specific cross-sectional configurations. In the subsequent process, the composite filament is split into finer single filament bundles through physical or chemical stripping methods, ultimately obtaining yarns composed of micrometer or even submicron fibers. The lower limit of yarn fiber fineness obtained by this method is difficult to control during the stripping process, and the cost is relatively high. The solution electrospinning method requires special dynamic collection devices (such as rotating funnels, parallel electrodes, rotating twisting devices, liquid baths, etc.) to orderly arrange, twist, and continuously collect and roll the sprayed nanofibers in order to form continuous yarns rather than non-woven fabrics[7]. This method has low yield, difficult control of yarn uniformity, and environmental pollution.

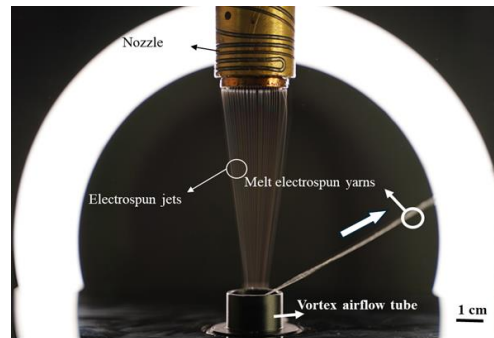


Fig. 1 In-situ fiber-forming process based on melt differential electrospinning [8]

We have developed a melt differential electrospinning in-situ spinning method to prepare yarns, which has significant advantages such as no need for solvents and efficient refinement of single fibers, with a simple process [8]. The PLA electrospun yarn prepared by this method was subjected to thermal drawing, low-temperature plasma treatment, and chitosan coating method to successfully prepare biodegradable antibacterial micro-nano fiber surgical sutures [9]. Under 1.6 times and 80 °C drawing, the average fiber diameter was 1.17 μm . The mechanical properties of the suture showed a trend of first increasing and then decreasing with the increase of stretching ratio and temperature. At 80°C and a draw ratio of 1.6, the fracture strength of the suture was 187.1 MPa. At this point, the fracture strength was nearly 2N, and the suture diameter was 117.6 μm , meeting the 6-0 surgical suture marking requirements. EDS showed that chitosan was evenly distributed on the surface of the fibers. After 24 hours of contact with cells, PLA-CS surgical sutures still had a cell survival rate of over 95% and a hemolysis rate of less than 5%. This proves that the suture has good biocompatibility and is expected to be used for functional surgical sutures.

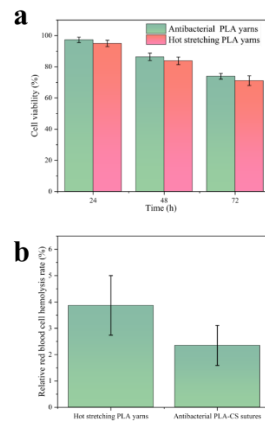


Fig. 2 Performance of PLA-CS surgical sutures [9]. (a) Cell survival rate; (b) Cell hemolysis rate.

C. Dura Mater Patches

The dura mater is a thick and tough bilayer membrane located between the skull and brain tissue, with the outer layer being the periosteum of the skull and the inner layer called the meninges. Defects or poor healing of the dura mater can lead to various complications. Repairing the dura mater is crucial for maintaining anatomical integrity and preventing complications such as epilepsy [10]. We prepared artificial dura mater patches using a differential nozzle with an inner conical surface. The detailed performance indicators showed that the artificial patches fully met the performance requirements of natural tissues and showed significant improvement in resistance to *Escherichia coli* and *Staphylococcus aureus* after meeting the requirements of carboxymethyl cellulose.

TABLE I. ARTIFICIAL DURA MATER PARAMETER TABLE

	Average thickness	Average diameter	tensile strength	elongation at break	porosity	Contact Angle
Human dura mater	200~400 μm	—	1.3~27.1 MPa	16%~49.7%	—	—
Melt different ial electros pun fiber membrane	Adjustable	2.04 μm	13.68 MPa	175%	74.42 %	144.27°

D. Anisotropic Cardiac Patches

Cardiac patches are of great significance for regenerating damaged myocardium and preventing end-stage heart failure. Their preparation should fully consider the anisotropy of natural myocardial cells, otherwise it may lead to increased electrical heterogeneity and cause arrhythmia [11].

we integrated MDES with Melt Electrowritten[12] (MEW) to produce anisotropic cardiac patches with structural features mimicking natural myocardium. Adjusting the angle of the stent can achieve anisotropy, approaching the natural myocardial structure, and the conductivity of the stent can maintain stability in the simulated in vivo environment.

The multi-layer composite structure is conducive to the adhesion and spreading of myocardial cells, and conductivity induces polar growth of cells, which is closer to the natural spindle morphology of myocardial cells.

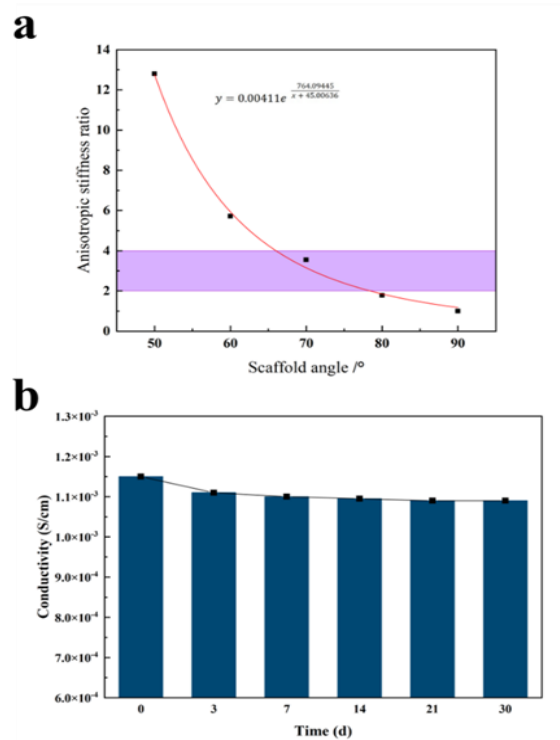


Fig. 3 Performance of anisotropic cardiac patch. (a) Anisotropic stiffness ratio; (b) Trend of patch conductivity over time.

III. SUMMARY AND OUTLOOK

MDES revolutionizes electrospinning by overcoming critical limitations of traditional methods. Key advantages include: Unprecedented Efficiency: 80× higher throughput than melt electrospinning and 500–1000× greater than solution electrospinning. Solvent-Free Process: Eliminates toxic solvents, reducing costs and environmental impact. Near-Perfect Material Utilization: Achieves ~100% polymer conversion vs. ~10% in solution methods. Precision Tuning: Adjustable fiber diameters (300 nm–5 µm) via multi-field coupling (electrostatic/thermal/aerodynamic).

Biomedical Application Domains advantages for: Advanced Drug Delivery Systems (e.g., transdermal patches). Implantable Medical Devices (sutures, dura mater repairs). Tissue-Engineered Constructs (anisotropic scaffolds like cardiac patches).

While MDES establishes a robust platform for biomedical innovation, future priorities include: Industrial Scaling: Bridging lab-scale efficiency to commercial production; Material Expansion: Adapting technology to broader polymer libraries (e.g., bioresorbable elastomers); Functional Hybridization: Integrating bioactive agents (growth factors, antimicrobials) during spinning; Dynamic Control: Developing real-time monitoring systems for fiber morphology/drug release; Clinical Translation: Accelerating in vivo validation of MDES-fabricated implants.

MDES positions electrospinning as a sustainable, high-precision manufacturing paradigm for next-generation biomedical solutions.

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**Biomechanical Performance of CFR-
PEEK Abutments and Crowns in a
Hybrid Dental Implant System: A 3D
Finite Element Analysis**

Biomechanical Performance of CFR-PEEK Abutments and Crowns in a Hybrid Dental Implant System: A 3D Finite Element Analysis

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Abstract

The significant difference in stiffness between titanium implants and bone causes occlusal forces to be transmitted directly to the surrounding tissue, potentially leading to damage and loosening of the implant. To reduce this issue, carbon-fiber-reinforced PEEK (CFR-PEEK) has been suggested as a more flexible option for abutments and crown. This study aims to estimate how a hybrid implant system incorporating CFR-PEEK components behaves under vertical and oblique loading. A 3D model, including bone and

a molar crown, was generated from a CT scan and integrated with an implant system (fixture, screw, abutment) designed in SolidWorks. Four finite element models were analyzed using ANSYS 16.0: (A) Titanium/Zirconia (Ti/Zr), (B) Ti/PEEK, (C) PEEK/Zr, and (D) PEEK/PEEK. A 200 N static load was applied both vertically and at a 45° oblique angle (buccal-lingual direction), and the resulting von Mises stress was evaluated. Under vertical loading, CFR-PEEK components absorbed stress within the prosthesis but increased stress on the retaining screw, raising the risk of loosening. Under oblique loading, stress in the cortical bone increased significantly (125 MPa) in all models. Furthermore, the PEEK abutments led to very high stress on both the screw and the abutment itself, reaching over 1300 MPa and 1480 MPa, respectively. This study concluded that although CFR-PEEK abutments can act as a flexible stress-modulating lever, they may cause mechanical failure of prosthetic components under the influence of oblique forces. Therefore, extreme caution should be exercised when using them in clinical situations involving significant axial forces.

Keywords— Dental Implants, Finite Element Analysis, CFR-PEEK, Biomechanical, Stress Distribution

I. INTRODUCTION

The long-term clinical success of implant-supported prostheses is critically dependent on both the development of advanced biomaterials and the optimization of biomechanical performance [1]. A central challenge in modern implant dentistry is the effective management of occlusal forces, which can be detrimental to the stability of the peri-implant bone interface [2,3]. Unlike the natural dentition, which benefits from the shock-absorbing capacity of the periodontal ligament, the direct, ankylotic connection in an

osseointegrated implant means that it lacks an intrinsic shock absorption mechanism [4]. Consequently, all occlusal forces are transmitted directly to the prosthetic components and the surrounding bone.

This issue is exacerbated by the significant mismatch in elastic modulus between rigid titanium (approx. 110 GPa) and native cortical bone (approx. 14-20 GPa) [5]. This disparity can lead to stress-shielding, concentrating forces in the crestal bone. Recent systematic reviews confirm that such occlusal overload is positively correlated with peri-implant marginal bone loss, establishing it as a significant clinical risk factor [6].

To address this biomechanical challenge, two primary advanced strategies have emerged. The first is an architectural approach, modifying the implant's internal structure through techniques like topology optimization to reduce its overall stiffness [7]. The second, and the focus of this study, is a material-based approach. This involves utilizing biomaterials with a lower elastic modulus. Carbon-fiber reinforced Polyetheretherketone (CFR-PEEK) has become a highly promising candidate due to its mechanical and physical similarities to bone tissue [8]. With an elastic modulus (approx. 18 GPa) that closely mimics cortical bone, CFR-PEEK has the potential to act as a stress-damper [8,9].

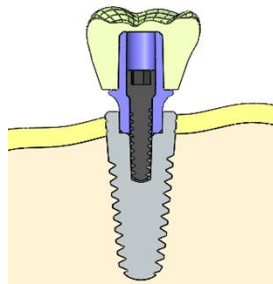
Finite element analysis (FEA) has become an indispensable tool for the preclinical biomechanical evaluation of such innovative concepts [10]. This study utilizes FEA to investigate combining a standard titanium implant fixture with a CFR-PEEK abutment to introduce a shock-absorbing element into the assembly. The influence of two different crown materials (Zirconia and CFR-PEEK) was also assessed under vertical and oblique loading conditions, building on previous work that highlighted the potential of this approach [11,12]. The aim of this study was to quantify the stress distribution in the

peri-implant bone and prosthetic components of this hybrid system. The null hypothesis was that there would be no significant difference in stress distribution when using a CFR-PEEK abutment compared to a conventional titanium abutment

II. MATERIALS AND METHODS

A. Model Generation

A patient-specific 3D model of a mandibular segment was generated from a Computed Tomography CT scan (DICOM format). The DICOM data was imported into medical image processing software (Mimics Research 21.0), where the cortical and cancellous bone were segmented based on Hounsfield unit thresholds. The resulting 3D masks were processed in 3-matic Research 13.0 to generate high-quality, 3D models (STL format). The bone STL model was imported into CAD software (SolidWorks Corp.). A conical, internal-connection implant fixture (5 mm diameter, 11.5 mm length) was virtually placed in the first molar region. A prosthetic abutment, retaining screw, and an anatomically realistic molar crown were designed and assembled onto the fixture (Fig. 1).



The model used in the study.

B. Material Properties and Methods

Four distinct finite element models were created. The implant fixture and retaining screw were consistently modeled as titanium alloy. The four experimental groups were: (A) Ti Abutment/Zirconia Crown, (B) PEEK Abutment/Zirconia Crown, (C) Ti Abutment/PEEK Crown, (D) PEEK Abutment/PEEK Crown. All materials were assumed to be homogeneous, isotropic, and linearly elastic. The specific material properties are detailed in Table 1 [13,14].

MECHANICAL PROPERTIES OF THE MATERIALS USED IN THE STUDY.

Material	Young's modulus (MPa)	Poisson's ratio
Titanium	110000	0.35
CFR Peek	18000	0.39
Cortical bone	13700	0.3
Cancellous bone	1370	0.3
Zirconia	210000	0.26

The nodes on the mesial, distal, and inferior surfaces of the bone block were fixed in all degrees of freedom. All interfaces between components were considered perfectly bonded. Two static load cases of 200 N were applied: (1) a vertical load on the occlusion surface and (2) an oblique load at 45° to the implant's long axis. The models were meshed in ANSYS 16.0 using 10-node tetrahedral elements. A mesh convergence study (<5% difference) was performed to validate the mesh. The final mesh consisted of approximately 1,470,708 nodes and 861,799 elements Fig.2. The von Mises equivalent stress criterion was used for eight analysis simulations, which are:

Model A (abutment TI and crown Zirconia) vertical loading

Model B (abutment PEEK and crown Zirconia) vertical loading

Model C (abutment TI and crown PEEK) vertical loading

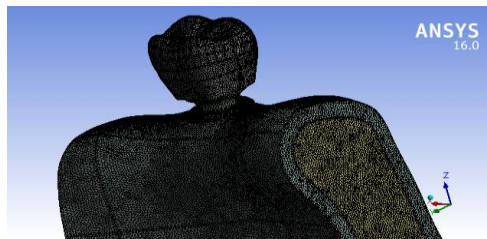
Model D (abutment PEEK and crown PEEK) vertical loading

Model E (abutment TI and crown Zirconia) oblique loading

Model F (abutment PEEK and crown Zirconia) oblique loading

Model G (abutment TI and crown PEEK) oblique loading

Model H (abutment PEEK and crown PEEK) oblique loading

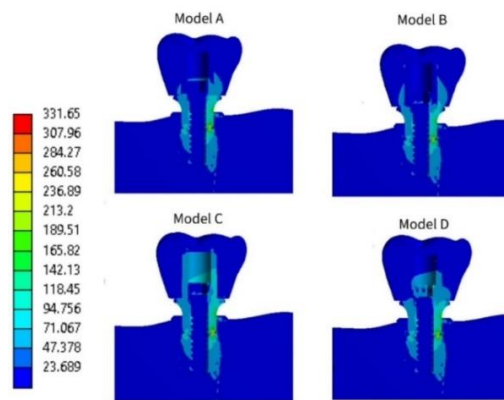


Finite element mesh of the model.

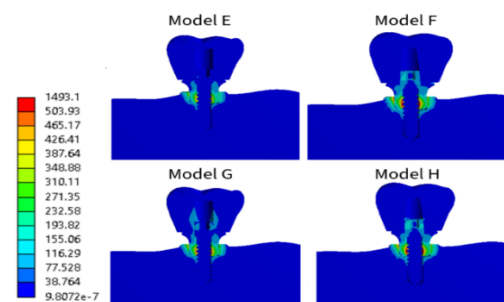
III. RESULTS

Table II, And III summarizes the maximum Von Mises stresses for all implant components for all simulations, while Figures 3 and 4 show the Von Mises stress distribution in cross-sections under vertical and inclined loads, respectively. Under vertical load (200 N), the maximum Von Mises stress in the peri-implant bone was low and similar across all four models (Models A to D). However, the stress in the cortical bone was constant for all models, and reaching 125 MPa. The use of a flexible CFR-PEEK crown (Models C and D) resulted in a concentration of stress within the crown and abutment. Notably, when using a CFR-PEEK abutment with a zirconia crown (Model B), the stress on the screw was six times greater (118.6 MPa) compared to the other models. When an oblique load of 200 N was applied, stresses

increased significantly in all components, in the cortical bone increased approximately six times in all models. The use of the CFR-PEEK abutment (models F and H) did not reduce this stress, but rather increased it. For example, for the screws, it increased from approximately 320 MPa to more than 1300 MPa, and for the abutment itself, it increased from approximately 975 MPa to more than 1480 MPa. The maximum stress was also concentrated in the implant components in the PEEK abutment models, rather than in the peri-implant bone in the Ti abutment models.



The Von Mises stress distribution in cross-sections under vertical loads



The Von Mises stress distribution in cross-sections under inclined loads

PEAK VON MISES STRESS VALUES (MPa) UNDER VERTICAL

Component	Model A	Model B	Model C	Model D
Cortical Bone	21.65	21.42	21.66	21.45
Cancellous Bone	3.54	3.54	3.54	3.45
Abutment	124.87	114.7	331.65	223
Screw	18.6	118.6	25.65	49.82
Fixture	119.5	62.11	119.54	118.58
Crown	39.73	55.99	321.08	225.9

PEAK VON MISES STRESS VALUES (MPa) UNDER OBLIQUE LOADING

Component	Model E	Model F	Model G	Model H
Cortical Bone	123.82	128.07	123.92	128.21
Cancellous Bone	6.45	6.18	6.46	6.19
Abutment	975	1484.3	978.75	1493.1
Screw	301.6	1309.3	341.49	1311.3
Fixture	1185.9	1364.9	1195	1368.6
Crown	208.5	227.19	368.63	338.64

IV. DISCUSSIN

The primary outcome of this study is the load-dependent biomechanical behavior of CFR-PEEK implant. While these

components demonstrated some ability to modulate stress under vertical loading, they created a critical and potentially detrimental biomechanical discrepancy under the more clinically significant oblique loads. The results challenge the notion that increased elasticity is always beneficial and reveal that the implant material is a key determinant of the failure pattern of the entire system, chart 1.

The significant increase in stress under oblique loading compared to axial loading highlights the importance of eccentric axial forces [3, 4, 6], chart 2. Under oblique loading, the implant and abutment assembly acts as a lever, pooling the applied force and generating a high bending moment. In previous studies using titanium steel (E and G), these moments translated into dangerously high stress concentrations in the cortical bone, aligning with reviews that correlate overload with marginal bone loss [5, 6]. one of the most important findings of this study is the effect of the CFR-PEEK abutment. Instead of reducing stress, the flexible PEEK abutment caused significant bending, resulting in significant stress concentrations on the internal components. The stress on the fixation screw exceeded 1300 MPa and the abutment 1480 MPa, which is greater than the yield stress of both Ti-6Al-4V and CFR-PEEK. This predicts mechanical failure such as screw loosening, abutment fracture, or even implant fracture, which are well-documented clinical complications. We conclude that the PEEK abutment did not protect the cortical bone under inclined loading, but rather caused a slight increase in stress. This is attributed to a flexion-compression mechanism, where the curved abutment causes its edges to compress the apical bone. This finding contrasts with studies on full PEEK implants [9] and highlights the unique interaction of the hybrid system.

Our study also demonstrates the hierarchical role of the components. The abutment material was the dominant factor determining the system's response to oblique loads, while the crown material had a secondary effect.

It is important to recognize the limitations of this finite element analysis study [10]. The model assumed perfect "bonded" contact at all interfaces, representing 100% osseointegration. The materials were modeled as linear and isotropic, while the bone was anisotropic. Finally, this study used constant loads. The real mastication cycle is dynamic, involving stresses over millions of cycles, a critical area for future research.

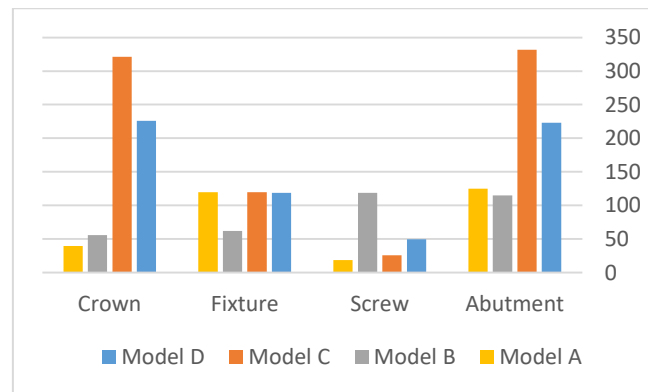


Chart 1: Show the Von Mises stress distribution in the dental implant component under vertical loads

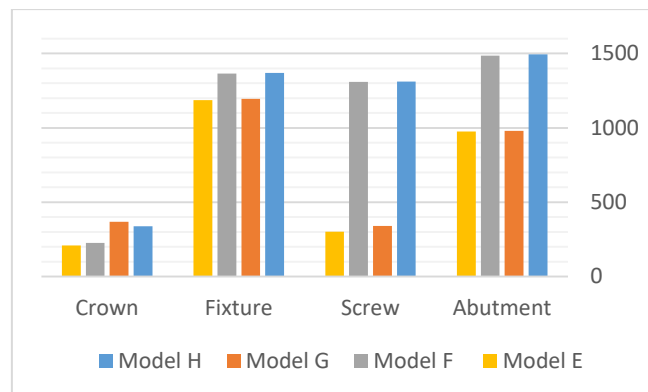


Chart 2: Show the Von Mises stress distribution in the dental implant component under inclined loads

V. CONCLUSION

This study demonstrates that although CFR-PEEK abutments can modify stress distribution within the implant under vertical loads, their biomechanical behavior under oblique loads is a significant problem. They radically shift the system's risk profile from potential biological failure (bone loss) to mechanical failure (component fracture), without providing the expected protection for the peri-implant bone. Abutment stiffness remains the most critical factor in maintaining the biomechanical integrity of an implant system under off-axial loads, and extreme caution must be exercised when using flexible abutments in areas of high occlusal stress.

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**Synthesis and Characterization of
Polymer-Like Thin Films on 304L Stainless
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Microwave (PECVD) Technique**

Synthesis and Characterization of Polymer-Like Thin Films on 304L Stainless Steel Used for Medical Application by Microwave (PECVD) Technique

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Abstract

Thin films were deposited on 304L stainless steel substrates (implant grade) using home-made microwave plasma enhanced chemical vapor deposition (PECVD) system with pure benzene (C_6H_6) as precursor gas and Argon for pre-cleaning process, at different parameters of deposition including working pressure, deposition time and negative bias voltage. The purpose of this research study is investigation of the effect of these parameters on the properties of the deposited thin films. The surface properties of the deposited thin film such as surface wettability and surface morphology were characterized by Contact Angle (CA) measured using Optical Tensiometer and Field Emission Scanning Electron Microscopy (FESEM), respectively. The corrosion behavior of the deposited thin film on stainless steel was evaluated by Electrochemical Impedance Spectroscopy (EIS). All the treated samples registered reduced CA below 90° ; their hydrophilic surfaces became more wettable. The deposition time had the greatest influence on the CA measured. It was observed that wettability can be adjusted by the plasma parameters, which would enable the production of coatings with properties suitable for specific practical applications, such as in biomedical devices (Implants). The collected (EIS) data

showed higher Z modulus of film coating at lower test frequency which indicated a better corrosion resistant of the metal substrate. The deposition process is more effective under working pressure 50 mTorr and 30 minutes deposition time.

Keywords— Thin film deposition, PECVD, CA, Wettability, EIS

I. Introduction

Biocompatibility is a fundamental requirement for any material implanted in the human body to avoid adverse effects such as inflammation, allergies, or toxicity. Furthermore, biomaterials must possess high corrosion and wear resistance in the physiological environment [1]. Ideal biomedical implants should have good mechanical properties coupled with a highly biocompatible surface [2]. Many medical devices, such as artificial hip and knee joints, coronary stents, and heart valves, are routinely implanted and come into contact with body fluids containing approximately 1% NaCl. This increases the likelihood of corrosion, which can have harmful effects on both the body and the implant. Consequently, developing chemical and biological stability in biomedical materials against corrosive body fluid environments is a widespread research interest [3,4]. Various materials are used in biomedical applications, including metals, alloys, polymers, ceramics, composites, and glasses [2,5]. For implants, the primary metals used are titanium-based alloys, cobalt-based alloys, and stainless steels [5]. The most common grades of stainless steel in this field are austenitic stainless steels (ASS) 316 and 304. ASS 304 is widely used in manufacturing and the nuclear, chemical, oil, petrochemical, and food industries, as well as in the medical industry for biomedical implants [6]. Stainless steel is inherently biocompatible, and its biocompatibility can be further improved by

modifying its surface energetics. The biocompatibility of a material is determined by the interactions between the implant and the biological system on the micrometer and nanometer scales, where physicochemical surface properties (such as chemical composition, wettability, and surface energy) play a critical role. There are different versions of stainless steel 304 with enhanced properties for specific applications, such as the low-carbon version 304L [7]. ASS 304L offers good corrosion resistance in many environments; however, it is susceptible to localized corrosion in the presence of chloride ions. While it provides greater resistance to intergranular corrosion than similar stainless steel grades in highly corrosive environments [7], it is prone to inter-granular corrosion in chloride environments due to precipitation of chromium as chromium carbide (Cr_{23}C_6) at grain boundaries. Although corrosion is inevitable, its rate of corrosion can be reduced through appropriate material selection and protective methods, such as: (a) using corrosion inhibitors, (b) applying protective films and coatings to the metal surface and (c) surface modification [8,9]. Surface modification is an effective method for tailoring bioactive components to meet clinical requirements [10]. It encompasses all types of surface treatments and coatings that alter the composition and the microstructure of the surface layer [2]. Over the past 40 years, plasma has become a highly useful tool for surface modification and deposition of various materials. Plasma Surface Modification (PSM) is an economical and an effective material processing technique used in the biomedical field due to its unique advantage of selectively enhancing surface properties and biocompatibility while leaving the bulk properties unchanged [11]. PSM can induce changes in the properties and chemical composition of a material's surface layer (such as wettability, adhesion, and biocompatibility), which has recently garnered significant interest from the medical field and is now used to improve the function and longevity of biomedical materials [4]. PSM of biomedical materials is

employed to clean surfaces, reduce thrombogenicity and cell/bacterial adhesion, eliminate protein adsorption, increase lubricity (by enhancing surface hydrophilicity i.e. wettability), alter transport properties, increase hardness, and enhance corrosion resistance [12]. PSM can be classified into three categories: plasma etching; plasma treatment and thin film deposition [2,11]. Thin film deposition technology is one of the oldest arts and, simultaneously, one of the newest sciences [2]. It is used to form layers in the thickness range of a few nanometers to about ten micrometers. Basically, thin-film deposition technology can be classified into three processes: purely physical, such as Evaporative Methods, purely chemical, such as Gas and Liquid Phase Chemical Processes and combine of physical-chemical such as Glow discharge processes [2,13]. Thin film deposition via glow discharge processes can be subdivided into: sputtering deposition and plasma enhanced chemical vapor deposition (PECVD) [14]. PECVD is highly efficient method for producing homogeneous organic thin films over large area substrates and offers good control over the film properties [15]. It is a green technology (i.e. environmentally benign) compared to other material processing methods. Additionally, it can occur at moderate temperature compared to conventional chemical reaction [4]. Recently surface modification via PECVD has attracted considerable interest in medicine and is now used to improve the function and longevity of biomedical materials [16]. Various sources are used for plasma generation in PECVD processes, with the most common being direct current (DC), radio frequency (RF) and microwave (MW) discharges. MW discharge is widely used for generation of cold plasma at pressures from 10^{-5} Torr up to atmospheric pressure (760 Torr) and at incident powers ranging from several watts to hundreds of kilowatts for different applications [17]. Magnetrons are the most common microwave generators due to their low cost and availability in the market for domestic use, such as in microwave ovens [5]. Several classes of the microwave plasma

generators exist, include the waveguide microwave plasma generator [18] which was used in this research. In this study, a home-made microwave plasma deposition system was used to deposit polymer-like organic thin films on 304L stainless steel substrates used in medical applications. Benzene and Argon were used as precursor and carrier gases, respectively. The effects of working pressure, deposition time and negative bias voltage on the surface properties of the deposited thin films (such as surface wettability and corrosion behavior) were investigated.

II. Material and Sample Preparation

A disc shaped of 304L austenitic stainless steel samples (biological grade) with 8 mm thick and 16 mm diameter were used for thin film deposition in this study. Its composition was determined by spark emission spectroscopy at the High Vocational Libyan Center of Casting at Tripoli. This alloy consists mostly of iron and about 17wt% chromium, 10wt% nickel and small amounts of other species as given in TABLE 1. All chemical composition values are quoted in weight percent (wt%) and represent the average of three measurements. The surfaces of the disc samples were wet ground on silicon carbide paper down to 2000 grit and then polished with alumina. Finally, they were cleaned in an ultrasonic bath using acetone and distilled water then dried just before loading into the deposition chamber.

TABLE 1. Chemical analysis of 304L stainless steel

Element	Fe	C	Mn	Si	Mo	Co	Cr	Cu	Ni	Others
wt%	69.4	0.0269	1.52	0.671	0.375	0.0699	17.0	0.361	10.1	0.576

A. Plasma Deposition System Procedure

A home-made microwave plasma deposition system, shown schematically in Fig. 1 (a), was constructed for the deposition of the polymer-like thin films. Fig. 1 (b) depicts the microwave plasma deposition system composed of (1) deposition chamber, (2) vacuum system, (3) and microwave generator (plasma source). The deposition chamber of stainless steel cylindrical vessel is provided with four ports: vacuum system, gas inlet, wave-guide and a glass window for observing the deposition process. The vacuum system consists of a turbo-molecular pump backed by mechanical pump and pressure gauges. The microwave is generated by the commercial magnetron (microwave furnace) at frequency of 2.45 GHz with maximum power of 900 W, which is transmitted to the chamber via a waveguide.

B. Plasma Deposition Procedure

After evacuating the chamber to a base pressure of ~ 0.1 mTorr, thin films deposited from benzene (C_6H_6) by microwave PECVD (see Fig. 2) on 304L stainless steel at various deposition parameters indicated in TABLE 2. Before deposition, pre-cleaning process with argon plasma was applied to both samples and chamber (as shown in Fig. 3) to remove any contaminations or organic oxides from the surface of samples and the chamber wall. This process was carried out at 180 watts of microwave power, base pressure of 0.73 mTorr and working pressure of 3.7 mTorr for 15 min. By adjusting these parameters, the nature and properties of deposited thin films were varied.

D. Characterization of Plasma Polymerized Films

The deposited thin films were analyzed by the following characterization techniques:

- Optical Tensiometer for contact angle measurements to analyze the surface wettability (hydrophilicity/ hydrophobicity).

- Field Emission Scanning Electron Microscope (FESEM) for surface morphology.

Electrochemical Impedance Spectroscopy (EIS) to evaluate the corrosion behavior of the polymer coated metals.

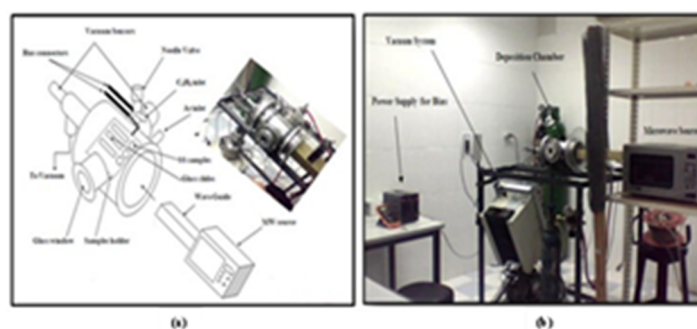


Fig. 1. (a) Schematic diagram and (b) Photograph of the home-made microwave plasma system

TABLE 2. Parameters of the Deposition Process

Parameter	Value
Power	540 W
Base pressure	~0.1 mTorr
Working pressure	10, 30, and 50 mTorr
Deposition time	5, 15, and 30 min
Bias voltage	-400 V

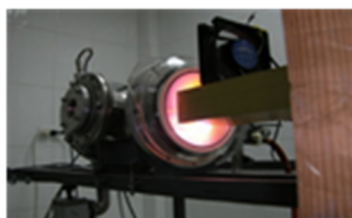


Fig. 2. Thin films deposited from benzene (C_6H_6) by microwave

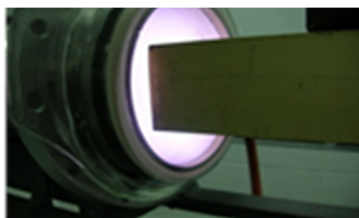


Fig. 3. Pre-cleaning process by Ar plasma before thin film deposition

III. RESULTS AND DISCUSSION

A. Surface Wettability

The hydrophobicity/hydrophilicity of a solid surface is usually expressed in terms of wettability that can be quantified by contact angle measurement [19]. A lower contact angle, higher Surface Free Energy (SFE) indicates good wettability i.e. more hydrophilicity. Conversely, a higher contact angle lower Surface Free Energy (SFE) means poor wettability i.e. more hydrophobicity. The surface wettability of the deposited thin films on the 304L stainless steel (SS) substrates was analyzed by measuring the water contact angle (WCA) on the thin films deposited from benzene at different deposition parameters, see Fig. 4. As can be seen in TABLE 3, the contact angle (θ^0) is lower than 90° for all the samples, and hence, they are classified as hydrophilic surfaces (i.e. wettable surfaces). Fig. 5 shows the effect of working pressure on WCA and SFE of the thin films deposited for 30 min. The WCA was decreased from 81° for untreated bare 304L SS surface to 33° and 30° for the deposited thin films at working pressures of 10 and 30 mTorr, respectively. But at 50 mTorr, the treated surface still registered a decrease in the WCA to 44° , this decrease was smaller than the others. On the other hand, the effect of deposition time on WCA and SFE of the thin films deposited at 50 mTorr. As can be seen; an increase in the deposition time led to a decrease in WCA and an increase in the SFE as

shown in Fig. 6. According to the results shown in TABLE 4, the deposition time seems to have a greater influence on the measured WCA and SFE when compared with the effect of working pressure.

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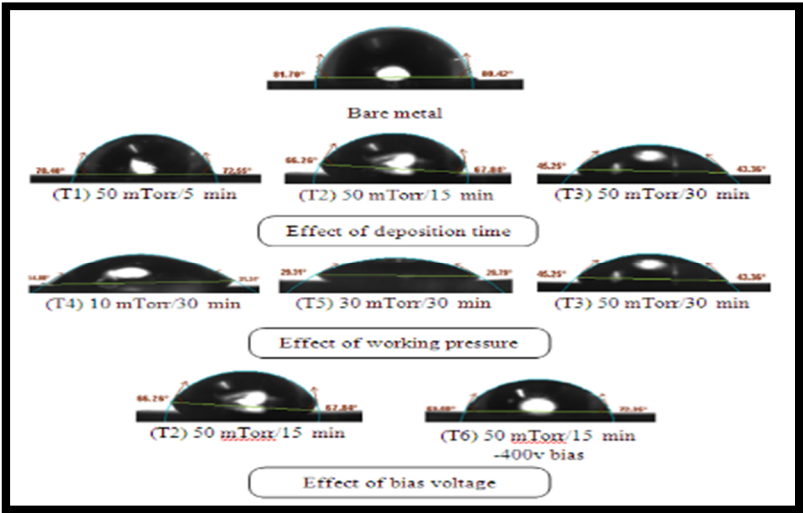


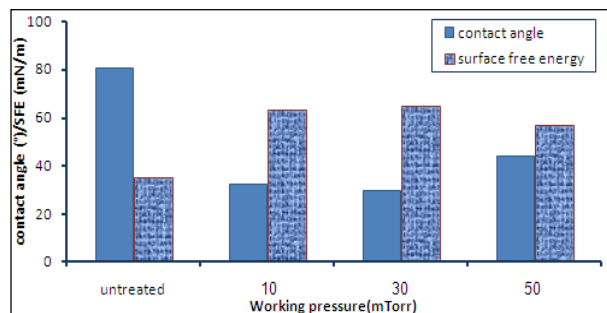
Fig. 4. Images of the measured water contact angle on the bare metal and deposited thin films from benzene at different deposition parameters

TABLE 3. Results of Contact Angle and Surface Free Energy Measurements.

Parameter Sample No	Working pressure (mTorr)	Time of deposition (min)	WCA* (θ°) [degrees]	SFE* [mN/m]	Remarks
Bare metal			81.20±0.88	35	
T1	10	30	32.61±0.56	63	Effect of working pressure
T2	30	30	29.84±0.60	65	
T3	50	30	44.35±1.10	57	
T4	50	5	71.48±1.11	46	Effect of deposition time
T5	50	15	67.18±1.31	49	
T3	50	30	44.35±1.10	57	
T5	50	15	67.18±1.31	49	No bias
T6	50	15	70.65±0.67	41	-400v bias

*SFE: Surface Free Energy

*WCA: Water Contact Angle

**Fig. 5. Effect of Working Pressure on WCA and SFE of the Thin Films**

Surface Morphology by FESEM Analysis

Fig. 7 (a,b) show the FESEM images of the untreated sample surface and the uniform thin films deposited at 50mTorr for 5min. Fig. 8 (a,b,c) depicted the effect of deposition time on the surface morphology of the thin film deposited. As deposition time increases, the surface morphology evolves from smooth (a) to rough (b) and fractured (c), highlighting the direct impact of time on thin film quality. These images provide valuable insight into the microstructural development of benzene films, which is crucial for scientific research applications. Fig. 9 (a,b) illustrate FESEM Images of the deposited thin films without and with pre-cleaning. The images result clearly demonstrate that plasma pre-cleaning plays a crucial role in enhancing the quality of the films deposited on 304L stainless steel. It improves

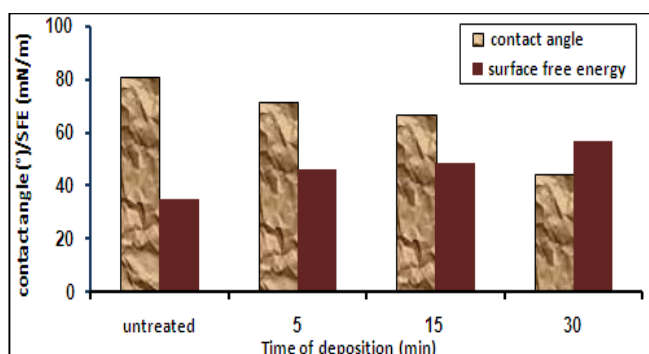


Fig. 6. Effect of Deposition Time on WCA and SFE of the Thin Films Deposited at 50 mTorr.

surface cleanliness and energy, leading to uniform nucleation, better adhesion, and a smoother film structure.

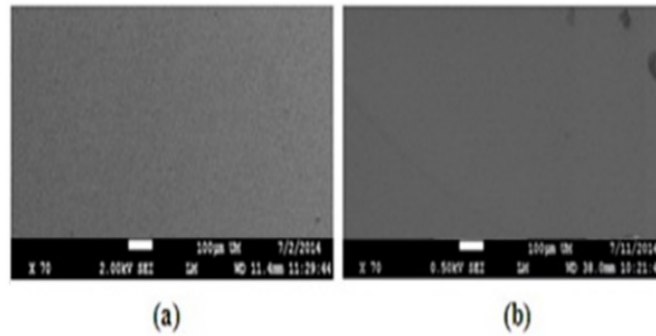


Fig. 7. FESEM Images of (a) Untreated Sample and (b) Uniform Thin Film Deposited at 50 mTorr for 5 min (X 70).

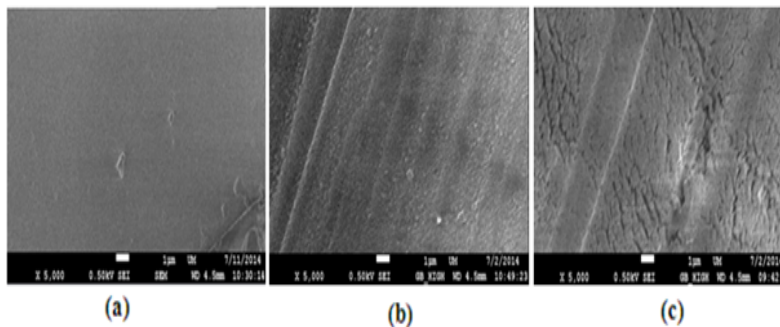


Fig. 8 (a,b,c). FESEM Images of Thin Film Deposited at 50 mTorr for Deposition Time of (a) 5 min, (b) 15 min and (c) 30 min (X 5,000).

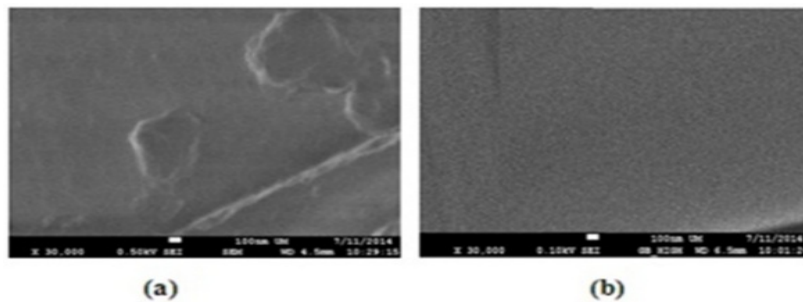


Fig. 9 (a,b). FESEM Images of Thin Film Deposited (a) Without Pre-cleaning (b) With Pre-Cleaning (X 30,000).

C. Electrochemical Characterization

The experimental setup for EIS measurement was shown in Fig. 10 which consists of three electrodes system. In addition to the stainless steel (working electrode), the corrosion cell has comprised counter electrode and reference electrode (Saturated Calomel Electrode (SCE)). Two types of corrosion measurements were conducted; open-circuit corrosion test survey in neutral chloride solution and an electrochemical impedance spectroscopy EIS. Impedance measurements were performed by applying a sinusoidal wave of 10mV amplitude to the working electrode. The frequency was stepped from 100kHz down to 10mHz. This measurement has been carried out in 3% NaCl electrolyte in order to determine compatibility and chemical resistance of deposited films. Fig. 11 (a,b) illustrate Open-Circuit Potential OCP measurement for coated stainless steel without and with pre-cleaning. In (a), the initial potential was about -138mV (SCE) and then drifts in the noble direction until it reaches nearly a



Fig. 10 Electrochemical Impedance Spectroscopy EIS

steady state condition at around -122mV (SCE) after 60 seconds of immersion in a 3% NaCl solution, while in (b), the open circuit potential starts at about -235mV (SCE) and drifts to about -180mV (SCE) after 60 seconds of immersion. By the end of this time period, there was no significant change in E_{corr} which is an indication that this specimen approaches a passive state with a minimum degradation rate. In both test results, the potential drift in the noble direction means that the film exposed to the test solution significant change in E_{corr} which is an indication that this specimen approaches a passive state with a minimum degradation rate. In both test results, the potential drift in the noble direction means that the film exposed to the test solution is resisting active dissolution.

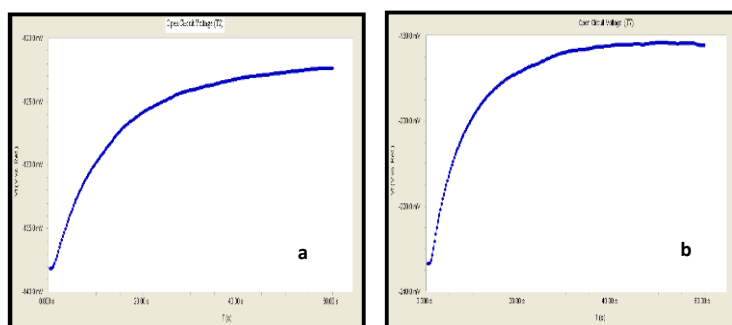


Fig. 11 Open-circuit potential measurement for coated stainless steel (a) without pre-cleaning and (b)

The electrochemical test results for impedance measurements are shown in Fig. 12 (a,b) as Bode and Nequist representation of impedance spectra respectively. Generally, higher Z modulus of the coating at lower frequency as shown in (a) indicates a better corrosion resistance. Also, the shape of the plot given in (b) gives an indication of the coating impedance behavior.

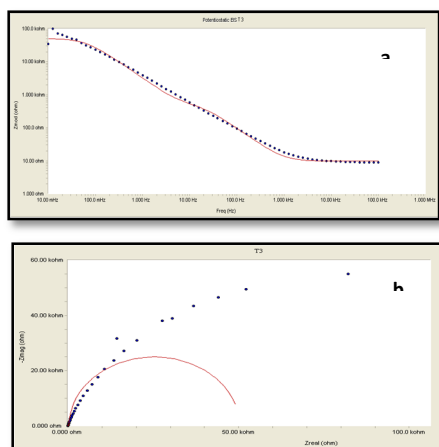


Fig. 12 Impedance data of coated stainless steel

Results of the fitting for the obtained spectra of the polymer-like coated stainless steel samples are plotted in Bode diagram to make a comparison of these spectra as shown in Fig. 13. As can be seen in the

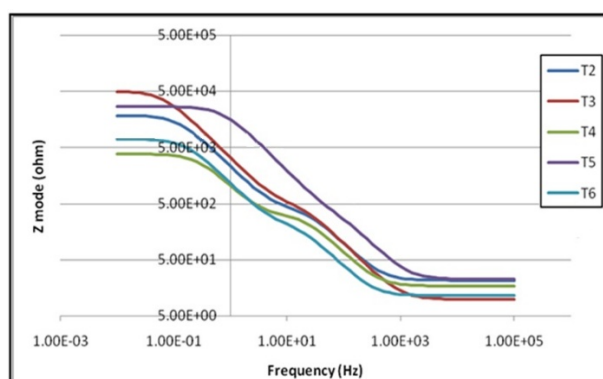


Fig. 13 EIS spectra of coated stainless steels at different deposition parameters

figure, it is possible to conclude that sample T3 has the highest value R_f ($\sim 50k\Omega$) while sample T4 has the lowest value ($\sim 3k\Omega$). So, the deposition process is more effective at 50mTorr working pressure and 30 minutes deposition time (sample T3) according to our home-made deposition system.

V. CONCLUSION

Thin films have been deposited on 304L stainless steel substrates at room temperature using benzene as a precursor gas by PECVD method. A microwave with frequency of 2.45GHz and 540W was applied for the ignition of the plasma. From this study, it can be concluded that stainless steel is inherently biocompatible, and its biocompatibility can be further improved by modifying its surface properties such as wettability and corrosion resistance. All the samples had a contact angle (θ) lower than 90° , so they are classified as a hydrophilic (i.e. wettable) surface. The wettability can be adjusted by the plasma parameters, which would enable the production of coatings with properties suitable for specific practical applications. Among test parameters of this study, time of film deposition was the most influential factor on the film surface wettability. The recorded higher (Z) modulus of film coating at a lower test frequency indicates better corrosion resistance to the metal substrate. According to the effect of deposition parameters, the deposition process is more effective at working pressure of 50mTorr for 30 minutes deposition time.

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**The role of biofluid mechanics in the
assessment and treatment of cancer
metastasis dynamics**

The role of biofluid mechanics in the assessment and treatment of cancer metastasis dynamics

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Abstract

The application of fluid mechanics principles to the field of cancer research has emerged as a promising approach to improve our understanding of tumor biology and develop more effective therapeutic strategies. This review focuses on analyzing the role of mechanical properties of biological fluids (e.g., blood, lymph, interstitial fluid) in the processes of tumor growth and metastasis, with special attention to the dynamics of cancer metastasis. The paper

discusses how fluid mechanics tools—such as computational simulations, microfluidics, and advanced imaging techniques—can be exploited to study the mechanisms of cancer cell spread and aggregation under forces such as shear stress, and to improve the design of tumor-targeted drug delivery systems. Despite encouraging progress, the review shows that important research gaps exist between in vitro models and in vivo physiological complexity, and highlights the need for further multidisciplinary integration to translate these biomechanical insights into clinical practice.

Keywords— Cancer metastasis, biofluid mechanics, shear stress, microfluidics, drug delivery, tumor microenvironment

I. INTRODUCTION

Fluid mechanics (fluid dynamics) forms a cornerstone in understanding many biological and medical phenomena. Its applications have contributed significantly to fields such as cardiovascular diseases (e.g., the study of blood flow and its relationship to atherosclerosis) [1], respiratory diseases (e.g., analysis of airflow in the lungs) [2], and in the design of precision drug delivery systems [3]. In recent years, these applications have expanded to include the field of cancer research, where studying the mechanical properties of biological fluids surrounding a tumor or transporting cancer cells provides profound insights into tumor behavior and spread.

Understanding the dynamics of cancer spread (metastasis) is a central challenge in oncology, as the vast majority of cancer deaths are due to complications from spread rather than the primary tumor. The formation of metastases goes through complex stages that include the detachment of cancer cells from the primary tumor, their invasion of surrounding tissues, their entry into the bloodstream or lymphatic system (intravascular spread), followed by their survival

in the circulation, their exit from the vessels (extravascular spread), and their settlement and growth at distant sites. At each of these steps, cancer cells interact with mechanical forces generated by fluid flow, affecting their fate [4]

This review aims to explore the critical role of biofluid mechanics in understanding and evaluating the dynamics of cancer metastases, and how this understanding can be harnessed to improve treatment techniques, especially drug delivery. The paper will provide an analysis of the techniques used (e.g. microfluidics and computational simulation), discuss current applications, focus critically on limitations and challenges facing the field, and suggest promising future research directions.

II. FLUID DYNAMICS IN CANCER

The flow of fluids in the blood and lymphatic vessels and the interstitial framework of the tumor exert mechanical forces on the cancer cells. The effect of these forces on the stages of propagation can be divided as follows ·

Invasion and detachment: The invasion of cells into the surrounding connective tissue is affected by the properties of the interstitial fluid and its pressure, as high interstitial pressure in the tumor is associated with difficulty in accessing drugs and increasing the possibility of cell proliferation.

Intravascular spread: When cancer cells enter the blood vessels, they are immediately exposed to shear stress forces resulting from blood flow. This stress can cause mechanical damage to vulnerable cells, acting as a natural filter, while cells able to withstand it may promote survival and proliferation pathways [5]

Transit in the blood circulation: Circulating cancer cells (CTCs) move with the blood stream. These cells often cluster together or with platelets or immune cells to form microemboli. This assembly increases their ability to withstand shear stress and protects them

from attack by killer immune cells (NK cells), and may also facilitate their entrapment in narrow capillaries [6]

Extravasation: When metastatic cells reach a capillary in a distant organ, they must attach to the vessel wall and penetrate it to exit. Here hydrodynamic forces play a role in determining the site of initial entrapment, while biochemical and mechanical interactions between the cell and vessel wall influence the efficiency of the penetration process.

Metastatic formation: After leaving the blood vessel, the cell must survive and reproduce in the new environment. Fluid pressure and tissue permeability in the “metastatic niche” affect the success of this crucial stage [7].

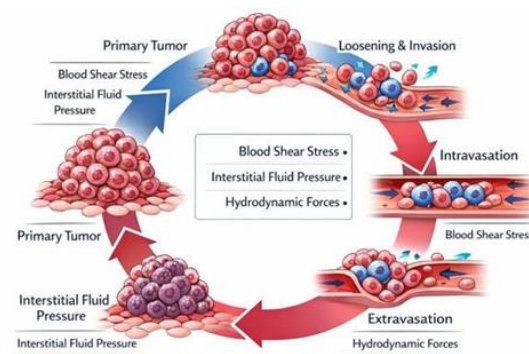


Fig. 1. The Role of Biological Mechanics in the Stages of Cancer Metastasis

III. APPLICATIONS OF FLUID MECHANICS TOOLS IN CANCER RESEARCH

A. Microfluidics devices

Microfluidic chips represent miniature laboratory platforms that simulate precise, controlled flow environments Used in modeling.

Microvascular environment: Channels with dimensions similar to capillaries are designed to study how circulating cancer cells respond to shear stress and their interaction with endothelial cells lining the vessels [8].

Extravascular diffusion process: Multilayer devices that mimic the blood vessel wall and surrounding tissue are designed to understand the mechanisms of cell penetration [9].

Screening for circulating tumor cells (CTCs): They are used as precise separation devices that rely on the physical properties (size, elasticity) of cells to separate and identify circulating tumor cells from patients' blood samples, providing valuable diagnostic information [10]

B. Computational Fluid Dynamics (CFD)

Simulation Computational modeling uses mathematics and algorithms to simulate the flow of fluids in complex systems.

Tumor vascular modeling: Digital models of irregular blood vessel networks in the tumor are built to predict blood flow patterns and drug diffusion within the tumor, which helps improve treatment strategies [11].

Drug carrier design: The movement and distribution of drug- carrying nanoparticles under the influence of blood flow is simulated to guide their design (size, shape, surface properties) to achieve maximum tumor targeting [12].

C. Improving the delivery of chemical drugs

The barrier to drug delivery to the tumor is a major challenge. Fluid mechanics helps in.

Magnetically directing drugs: Using magnetic nanoparticles and external magnetic fields, the drug concentration can be directed toward the tumor more precisely, reducing side effects [13]

Enhanced infiltration and retention (EPR Effect): Understanding the hemodynamics of tumor leaking vessels helps improve the design of nanoparticles to take advantage of enhanced infiltration and retention

Despite great potential, the application of fluid mechanics in clinical oncology faces fundamental obstacles:

- **Physiological complexity:** The vivo tumor environment is characterized by extreme heterogeneity in vascular structure, pressure, and mechanical properties of the tissue. Current laboratory and computational models are often simplistic and cannot capture this full complexity.
- **Scalability limitations:** Results obtained from very small microfluidic models may be difficult to transfer to real human body dimensions and processes (scalability).
- **The gap between models and clinical reality:** Most research is still in the laboratory or theoretical modeling stage. Further preclinical (animal) and clinical studies are needed to prove efficacy and safety.
- **Ethics and regulatory challenges:** Applying new technologies such as targeted nanocarriers or biophysical therapeutics requires overcoming stringent regulatory procedures and proving their clear superiority over standard treatments with an acceptable safety profile

IV. Future Perspective and Proposed Frameworks

To develop this field, the authors suggest focusing on:

1. **Development of multi-scale models:** Integrating microfluidic models with 3D systems (such as bioscaffolds or organs-on-a-chip) for more realistic simulation of the multi-cellular and multi-tissue metastatic environment.

2. Integrating with systems biology: linking mechanical data (such as shear stress) to molecular and genetic responses within the cancer cell to understand the underlying mechanisms.
3. Advanced imaging and biomedical technologies: Leveraging techniques such as flow cytometric magnetic resonance imaging (PC-MRI) [14] to obtain real dynamic data from patients to enrich computational models and improve their predictive accuracy.
4. Developing clinical predictive frameworks: The ultimate goal is to build personalized computational models that use patient imaging and biometric data to predict patterns of tumor spread and select optimal treatment based on fluid mechanics principles

V. Conclusion

Applying the principles of biofluid mechanics provides a unique lens to decipher the complexity of the dynamics of cancer metastasis. Tools such as microfluidics and computational simulations have enabled researchers to investigate the mechanical forces that control the fate of circulating cancer cells, and have opened new horizons for designing smarter, targeted therapies. However, the road to broad clinical application is still long and requires bridging the gap between simplified laboratory models and the physiological complexity of the human body, overcoming technical and regulatory challenges. The deep integration of engineering, physics, cancer biology and clinical medicine is key to turning this promising vision into a therapeutic reality that improves the lives of cancer patients.

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**Fiber-Reinforced Composites for
Dental Applications: A Review**

Fiber-Reinforced Composites for Dental Applications: A Review

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Abstract

Fiber-Reinforced Composites (FRCs) are advanced nonmetal materials composed of high-strength fibers (such as glass, carbon, or aramid), that are embedded in polymer matrix. In dentistry, FRCs provide high tensile strength, fatigue resistance, and a modulus of elasticity comparable to dentin and bone, thus ensuring biomechanical compatibility. Their translucency, corrosion resistance, and conservative application offer good advantages over traditional metal-based restorations. FRCs are extensively used in modern clinical dentistry for a wide range of applications, such as fixed prosthodontics, orthodontics, periodontology, and restorative procedures, including resin-bonded prostheses, posts, retainers, splints, and denture reinforcement. Despite these advantages challenges remain, such as technique sensitivity, uncertainties

regarding long-term repetitive loading performance, and difficulties in fiber impregnation. To overcome these issues, recent innovations include the incorporation of nanofillers, advanced fiber architectures, and bioactive surface modifications, which have significantly enhanced clinical outcomes and reliability. Current evidence increasingly supports the long-term success of FRCs, reinforcing their role as a promising alternative to metals in restorative dentistry. With ongoing progress in adhesive technologies and materials science, FRCs are expected to expand their applications, particularly in treatments requiring durability, esthetics, and conservation of tooth structure. This review highlights the composition, mechanical properties, esthetics, and current clinical applications of FRCs. Overall, FRCs represent a versatile and evolving class of dental biomaterials that align functional strength with esthetic demands, ensuring a growing role in modern restorative and prosthetic dentistry.

Keywords: synthetic fibers, resin matrix, composites, mechanical properties, dental applications.

I. INTRODUCTION

Fiber-reinforced composites (FRCs) are synthetic, lightweight, metal-free materials that have been used in various engineering [1, 2] and biomedical applications since the 1960s [3, 4, 5, 6]. Conventional dental composites are increasingly being reinforced with fibers to improve their clinical longevity and durability [7, 8, 9]. The incorporation of fiber into the resin matrix has shown improvements in the mechanical properties [10, 11]. Fiber addition can increase the flexural strength, modulus of elasticity, and impact strength of dental composites [12, 13, 14, 15, 16, 17]. Furthermore, it also enhances other essential properties, including hardness [18], resistance to water absorption [19], fatigue resistance [12, 20], and fracture toughness

[17, 21]. Various types of fibers have been investigated for their potential use as reinforcements in PMMA denture bases [22, 23, 24, 25].

FRCs are structurally composed of strong reinforcing fibers embedded within a resinous matrix. The fibers are distinguished by a high aspect ratio (length-to-diameter) [26]; they primarily impart tensile strength and stiffness [1]. The surrounding matrix contributes to the material's toughness, dimensional stability, and overall structural integrity [8, 27, 2]. The reinforcing fibers and the matrix (which acts as a binder) are the major constituents of FRCs [28]. Other minor constituents may include coupling agents, coatings, and fillers [8]. Coupling agents are added to enhance the chemical bonds between the fiber and the matrix resin, thereby facilitating a better load transfer between the fibers and the matrix [27]. Additionally, the fillers are sometimes incorporated into the polymeric matrix primarily to reduce cost and improve their properties [2, 8, 29]. Several critical factors influence the performance of FRCs, such as the type of fiber (e.g., Glass, Carbon, Polyethylene, or Aramid) [27, 30], its length and geometry [23], orientation [8, 13, 23], the volume fraction of the fibers [10, 31], and the bonding efficiency at the fiber-matrix interface [1, 10, 12, 16, 31, 32, 33].

FRCs have significantly advanced restorative dentistry and have gained rapid clinical popularity due to continuous material developments that enhance their suitability for oral applications [9,14]. Innovations in fiber materials, resin matrices, and bonding agents have led to improved mechanical properties and long-term clinical performance [34, 35, 37]. Furthermore, the development of pre-impregnated fiber systems has greatly simplified handling and placement for clinicians [14, 36]. Among the different types of dental FRCs [9,15], their primary advantage is their ability to undergo

silanization, a surface treatment that promotes strong, covalent chemical bonds with the monomers and dimethacrylates, such as bisphenol A-glycidyl methacrylate (Bis-GMA), urethane methacrylate (UDMA), and triethylene glycol methacrylate (TEGDMA), of the polymer resin matrix [14, 34, 35, 33]. This robust interfacial adhesion, combined with their superior mechanical strength, biocompatibility, and translucent esthetic qualities, establishes glass fibers as the leading choice for modern dental restorations [14, 15, 26, 34, 35].

FRCs are widely used for a variety of applications in dentistry, such as fixed partial dentures (FPDs) [8, 7, 37, 38], periodontal splints [3, 8, 39], endodontic posts [40], orthodontic retainers [28], reinforcement for denture bases [20, 22, 24] and implant prostheses [32]. Their ability to customize properties allows restorations to be precisely tailored to specific clinical needs [4]. The successful clinical outcome of an FRC restoration depends on careful material selection [26], guided by the intended application [8], anticipated functional load demands [37, 41], and esthetic considerations. As research continues, the development of novel fiber systems with superior properties is expected to further improve the clinical performance of FRCs [37], thereby expanding their role in creating durable and esthetic dental prostheses for the benefit of both patients and practitioners [9, 42]

II. FIBER TYPES

The development of FRCs represents a significant advancement in dental material technology, where various fibers are incorporated into a resin matrix to enhance the properties of conventional dental composites [13, 22, 32]. The most widely investigated and practiced fiber types in dentistry are polyethylene [12], glass [14, 33], carbon [12], and aramid fibers [8, 36], all of which have demonstrated effectiveness in strengthening dental resin composites.

The main advantages of FRCs compared with conventional restorative materials include ease of handling and superior mechanical performance, particularly under dynamic loading conditions [37]. In many clinical situations, FRC restorations require minimal or no laboratory procedures, as frameworks can often be fabricated directly at the chairside [26]. Another significant benefit of these materials is their superior esthetic outcome compared to metal-reinforced alternatives [32]. Moreover, the complete absence of metallic components in FRC structures makes them suitable for patients with metal hypersensitivities, such as nickel allergies, and allows their safe use in individuals who require magnetic resonance imaging [43].

A. Glass fibers:

Glass fiber reinforced composites (G-FRCs) are a popular choice in both industrial [44] and dental fields [45] due to a unique combination of properties. They exhibit exceptional mechanical strength, including high tensile, fracture, impact, and compressive strength, along with a high modulus of elasticity that provides superior stiffness and dimensional stability [16, 19]. Furthermore, their esthetic transparency, biocompatibility, and low cost significantly contribute to their widespread use in esthetic dental restorations [44, 45].

The most common type of reinforcing fiber is glass fiber, which is available in various compositions, including E-glass, S-glass, A-glass, C-glass, D-glass, and AR-glass [2, 6, 46]. The orientation of these fibers is a critical factor that significantly enhances the composite's performance [22, 47]. While their tensile strength can reach 7000 N/mm² under laboratory conditions, commercial-grade fibers typically offer strengths in the range of 2800-4800 N/mm² [36, 48].

The profound reinforcing effect of G-FRCs has been well-documented. For instance, studies have shown that G-FRCs can increase the flexural strength of unreinforced composites 364% after water storage and up to 800% under dry conditions [10, 19]. This

robust performance makes them widely accepted for dental restorations, prostheses, and appliances that endure significant occlusal loads [41], such as post-endodontic restorations [40], crowns [8], fixed partial dentures (*FPDs*) [37, 38, 49], root canal posts [8, 40], and orthodontic retention devices [28].

The clinical success of G-FRCs in dentistry depends on optimizing several fiber characteristics. These factors include the composition [8], diameter [26], length, quantity, orientation, and distribution of the fibers [10, 50], as well as their adhesion and impregnation within the resin matrix [33]. When these variables are tailored to specific clinical needs, G-FRCs provide reliable and effective reinforcement for dental appliances [34, 50].

Table I. Mechanical & Physical Properties of Glass Fiber

Type	Density (g/cm ³)	Tensile Strength (GPa)	Young's Modulus (GPa)	Elongati on (%)
E-glass	2.59	3.446	72.31	4.7
C-glass	2.53	3.32	68.94	4.6
S-glass	2.45	4.88	86.92	5.5
A-glass	2.43	3.30	68.99	4.9
R-glass	2.56	4.133	85.58	4.9
EC-glass	2.74	3.446	85.57	4.7
AR-glass	2.72	3.242	73.11	4.5

B. Carbon fibers:

Carbon fibers (CFs) are advanced materials valued for their low density [12], high tensile strength, chemical stability, and

biocompatibility [6], making them highly suitable for biomedical applications such as orthopedic prostheses [51] and radiological support devices. Typically manufactured from precursors like polyacrylonitrile (PAN), rayon, or pitch, CFs consist of thousands of parallel filaments, each 5-10 μm in diameter and composed almost entirely of carbon atoms [52]. Technological advancements have led to the development of carbon nanofibers, which significantly enhance the performance of conventional biomaterials. These nanostructures have opened new possibilities in regenerative medicine and oncology, finding use as scaffolds for bone tissue engineering [6, 53], tendon and ligament repair, and as suture materials for hernia reconstruction [6].

In dentistry, carbon fibers (CFs) have been used since the 1980s to reinforce prosthetic frameworks and denture bases, improving their fatigue resistance and impact strength [12, 15, 54]. A notable application is in dental posts, where continuous unidirectional carbon fibers are embedded in an epoxy matrix [55]. The advantage of these posts is their lower elastic modulus compared to metals, allowing for more even stress distribution within the tooth root and reducing the risk of fracture [8, 55]. However, their clinical use is limited by significant drawbacks, including a lack of radiopacity and a black coloration that compromises esthetics, particularly under all-ceramic crowns [55].

C. Kevlar fibers

Kevlar is a para-aramid fiber introduced in the 1960s, offers several advantages including low density, high tensile strength, toughness, stiffness, and thermal stability. This unique combination of properties makes it a preferred material in demanding sectors such as aerospace, automotive, protective textiles, sporting goods, and biomedical applications [27, 30, 56, 57]. Modern composite technologies have

expanded Kevlar's utility. Methods include creating hybrid composites by combining Kevlar with fibers like carbon or glass to improve impact resistance [1] and incorporating nanofillers such as graphene, to enhance mechanical properties and fiber-matrix adhesion [5, 58]. These advanced nanomodified composites show great potential as smart structural systems due to their enhanced toughness and energy absorption [29, 59].

In dentistry, Kevlar is an emerging reinforcement material, primarily because its modulus of elasticity is similar to that of dentin. This property allows for favorable stress distribution, reducing crack propagation and improving the fracture resistance of endodontic posts and restorative systems. The main challenge is achieving strong adhesion, which has been addressed in research through surface treatments. For example, one study successfully developed a Kevlar intracanal post by treating the fibers with acetic acid and a silane coupling agent, resulting in a composite with suitable mechanical strength, fatigue resistance, and biocompatibility [8]. Despite these advances and its historical use in strengthening acrylic dentures [8, 15], Kevlar's primary limitation for broad dental application remains its intrinsic yellow color, which compromises esthetic requirements [8, 57, 60].

D. Polyethylene fibers

Polyethylene Fiber Reinforced Composites (PE-FRCs), also known as Ultra High Molecular Weight Polyethylene (UHMWPE), have been commercially available since the 1990s. These fibers are manufactured via gel-spinning to create highly crystalline, oriented fibers with a high strength-to-weight ratio [8, 16]. Commercial examples include Ribbond, Spectra, and Dyneema. PE-FRCs feature three-dimensional architectures (e.g., leno-weave) that improve mechanical interlocking and stress distribution [8, 61]. Surface

treatments by plasma and silane are often used to improve adhesion to the resin matrix [11, 33].

The Ribbond system (PE-FRC) is one of the most widely used options in dentistry. Its characteristics include being biocompatible, chemically inert, colorless, and flexible [8]. It significantly increases fracture toughness [11], redistributes stress, and provides an excellent option for creating conservative, highly esthetic bonded restorations [8, 30, 62, 63].

Previous studies have confirmed that polyethylene fiber significantly increases fracture strength [16], fracture toughness, reduce marginal leakage, and promote more favorable fracture patterns compared with conventional composites [11, 62, 64]. Ribbond's flexibility and lace-like design allow it to easily adapt to cavity walls, enabling dentists to apply multiple layers for reinforcement [8]. When combined with modern adhesive systems and high-strength composites, PE-FRCs enable the creation of conservative and highly esthetic bonded prostheses without the need for extensive tooth preparation [30, 63].

III. FIBER ORIENTATION

The fiber content in a polymer matrix typically ranges from 40 to 65 vol % [65]. This range is crucial for ensuring optimal performance, as it balances two requirements: sufficient reinforcement and matrix integrity. If the fiber content is below 40 vol %, the material behaves like the weaker polymer matrix. Conversely, if the content is above 65 vol %, it becomes difficult for the viscous resin to achieve complete wetting of all the fibers. This incomplete wetting creates voids and porosity that act as stress concentrators and compromise the critical fiber-matrix interfacial bond, leading to reduced fatigue resistance and overall strength [10, 66]. Therefore,

maximizing the material properties requires maintaining this optimal volume fraction alongside effective surface treatments [11, 67].

Table I. Classification Of Dental Frc Products [30]

Product	Company	Fiber Type & Fiber architecture
Pre-impregnated dental	laboratory	products
FiberKor	Jeneric/ Pentron	Glass/ Unidirectional
Vectris pontic	Ivoclar	Glass/ Unidirectional
Vectris frame and single	Ivoclar	Glass/ Mesh
Pre-impregnated dental	chairside	products
Splint-It	Jeneric/ Pentron	Glass/ Unidirectional
Splint-It	Jeneric/ Pentron	Glass/ Weave
Splint-It	Jeneric/ Pentron	Polyethylene/ Weave
Impregnation required	chairside	products
Connect	Kerr	Polyethylene /Braid
DVA fibers	Dental Ventures	Polyethylene/ Unidirectional
Fiber-Splint	Inter Dental Distributors	Glass/ Weave
Fiberflex	Biocomp	Kevlar/ Unidirectional
GlasSpan	GlasSpan	Glass/ Braid
Ribbond	Ribbond	Polyethylene/ Leno, weave
Pre-impregnated	prefabricated	posts

C-post	Bisco	Carbon/ Unidirectional
Fiberkor	Jeneric/ Pentron	Glass/ Unidirectional

IV. FIBER PROPERTIES

Nowadays, many studies are focused on enhancing the physical and mechanical properties of FRCs, and various techniques have been developed to improve their performance [37]. The reinforcement is often achieved by incorporating nanoparticle fillers such as silicon dioxide (SiO_2) [29], zirconium dioxide (ZrO_2), titanium dioxide (TiO_2), zinc oxide (ZnO), hydroxyapatite ($\text{Ca}_5(\text{PO}_4)_3(\text{OH})$), and fibers into the resin matrix [24].

The mechanical behaviors of FRCs for biomedical applications are mainly dependent on their inherent abilities to enable stress transfer [68]. Furthermore, this performance depends on fiber type [30], quantity, and fiber orientation within the matrix [65, 68]. The improvement in composites' characteristics can be achieved through proper selection of fiber type, concentration (volume fraction) in the matrix [69], pre-impregnation [36], and silane treatment of fiber surface to strengthen the interfacial adhesion between the fiber and matrix [2, 8, 70, 33]. Moreover, the reinforcement benefits are primarily obtained by means of the greater length of the fibers compared to their cross-sectional diameter [20, 26, 49].

FRCs are characterized by their low density, high stiffness [26, 71], corrosion resistance, favorable esthetics [32], and superior strength-to-weight ratio compared to conventional materials such as metal alloys [2,5,72]. Their mechanical strength and elastic modulus often closely match those of natural bone [6] and dentin [8], which makes them highly suitable for biomedical applications [24].

TABLE III. Mechanical Properties of FRCs

Properties	FRCs
Compressive strength (MPa)	260 -300 [8]
Yield stress (MPa)	160 -300 [49]
Tensile strength (MPa)	40 -50 [73]
Flexural strength (MPa)	80 -150 [73]
Modulus of elasticity (GPa)	6 -14 [49, 73]
Hardness (VHN)	30 -90 [8, 73]

II. FIBERS IN DENTAL APPLICATIONS

The application of FRCs in dentistry has expanded considerably in recent years because of their favorable strength-to-weight ratio [2, 8, 74], biocompatibility, and low cost [8]. FRC technology offers potential solutions to the limitations of metal alloy substructures, including issues of corrosion, toxicity, complex fabrication, high cost, and compromised esthetics [75]. These composites are now widely used in fixed prosthodontics, for applications ranging from conventional laboratory fabricated restorations to minimally invasive chairside treatments [3, 4, 76]. Their clinical applications include bridges [8], splints [23], orthodontic retainers [28], and implant prostheses [32]. Their uses also extend to posts [8], denture bases [22], clasps [77], connectors, and space maintainers [78, 79]. The combination of adhesive bonding strategies with the flexibility of adjusting fiber orientation supports a conservative, tooth-preserving restorative approach [3, 4]. Additionally, the translucent and non-

corrosive characteristics of glass and silica fibers provide superior esthetic outcomes compared to traditional metal frameworks [32, 77]. These properties, including durability, favorable modulus of elasticity [8], and cosmetic advantages, have established FRCs as a dependable and versatile material in contemporary dental practice.

TABLE IV: Main Clinical Applications Of Frcs In Dentistry.

Specialty	Clinical use
Prosthodontics	Provisional or definitive fixed dentures, prostheses, veneers, direct or indirect pontics, and repair of removable devices [9, 23, 37, 38]
Endodontics	Prefabricated or customized root canal anchoring systems [8, 9, 40]
Conservative dentistry	Direct and indirect fillings, inlays, and overlays [8, 9]
Orthodontics	Retention splints, space maintainers, active en-masse units, metal-free brackets, and orthodontic wires [9, 28, 80]
Periodontology	Periodontal splints and posttraumatic splints [8, 9, 39]
Paediatric Dentistry	Crowns in primary molars, splints, space maintainers, and direct fillings [9, 28]

A. Prosthodontics

FRCs are essential support materials in prosthodontics, particularly for reinforcing removable acrylic dentures [22]. The fiber framework incorporated into the denture base has been shown to significantly

enhance both the impact and flexural strength [13, 20]. Furthermore, the use of anatomically customized E-glass short fiber posts has been shown in vitro studies to improve mechanical properties in weakened, endodontically treated premolars, demonstrating better adaptability and strength in compromised teeth [33, 50, 81]. Moreover, randomized clinical trials conducted on endodontically treated teeth indicate that the use of polyethylene fiber-reinforced composites provides significantly better resistance to fracture and improved longevity when compared to traditional composite restorations [8, 30, 63].

B. Pediatric Dentistry

In pediatric dentistry, FRCs are a versatile metal-free option for various clinical applications, including restorations [8], post-traumatic splinting [39], and the fabrication of space maintainers [28]. FRCs have demonstrated excellent clinical performance and durability in the pediatric population [9, 82]. For traumatized teeth, FRC splints provide clinically effective stabilization. Although concerns about excessive rigidity exist, modern techniques such as spot-bonding can be used to reduce splint rigidity and allow for physiologic tooth movement, thereby minimizing the risk of ankylosis [39]. FRCs are also ideal for fabricating esthetic, lightweight, and durable space maintainers following the premature loss of primary molars [28]. Although the enamel of primary teeth differs significantly from permanent enamel in terms of composition, mechanical properties, and bond strength [80], FRC devices have nonetheless shown acceptable clinical performance, durability, and ease of use in children [9, 84, 85]. These materials are particularly valuable for treating traumatized teeth, where FRC splints provide effective stabilization to avoid excessive rigidity; such techniques as spot-bonding are employed to allow for physiologic tooth movement and minimize the risk of ankylosis [39]. Overall, FRCs have demonstrated excellent

clinical performance and durability within the pediatric population [82].

C. Orthodontics

The principal use of FRCs in clinical orthodontics is the fabrication of fixed lingual retainers to ensure crucial long-term stability that is crucial for maintaining treatment results [7, 86]. These bonded retainers are well accepted by patients and are relatively independent of patient cooperation [28, 86]. Clinical findings confirm that FRC retainers provide sufficient bond strength to both enamel [30, 87] and dentin [80,88], and demonstrate good clinical reliability over moderate follow-up periods [89]. A major advantage FRC retainers hold over traditional metallic wires is superior esthetics, as the fibers are almost invisible and do not affect the natural translucency of the teeth [3, 4]. This esthetic superiority is particularly important because of the higher number of adult patients seeking orthodontic treatment. Furthermore, FRCs are metal-free, making them suitable for patients undergoing Magnetic Resonance Imaging (MRI) [43] or those with metal allergies [75]. A potential drawback is that FRC splints can be more rigid than conventional metallic splints, which increases the risk of ankylosis of the involved teeth. However, the use of a spot-bonding technique has been suggested to counteract this by reducing framework rigidity and allowing for necessary physiologic tooth movement [39]. Beyond retention, FRCs have other clinical uses: they are successfully applied as space maintainers to prevent space loss following the premature removal of deciduous molars [28, 90]. Moreover, these space maintainers can be efficiently prepared on plaster models and bonded directly to adjacent teeth [91]. Additionally, FRCs have been investigated for active tooth movement, where groups of two or more teeth are splinted together and moved *en masse* using sectional mechanics [28, 32, 92]. FRCs have also been

investigated as innovative materials for the fabrication of orthodontic brackets [9].

D. Periodontology

FRCs are widely utilized in periodontics for splinting teeth that have become mobile due to bone loss or trauma [8, 9]. The core objective of these splints is to stabilize the teeth, effectively reducing mobility and improving patient comfort [93]. FRC splints have demonstrated reliable long-term stability [94] and possess higher flexural strength compared to conventional metallic wire splints [39, 95]. The clinical advantage is the ability to fabricate these splints intraorally in a single appointment, as FRCs show high flexural resistance even when cured chairside without post-polymerization in a laboratory oven, thus simplifying the overall treatment protocol [3, 4, 8]. The most common failures are debonding and fracture, particularly when splinting teeth with varied degrees of mobility, as differential mobility is a primary risk factor [39]. However, a significant benefit is that FRC splints are easily repaired intraorally, often negating the need for complete replacement [30, 39, 96, 97].

In Implant Prosthetics, FRCs are highly effective as framework design materials, particularly in conjunction with short implants [37, 97]. Studies have found that using four ultra-short implants with FRC prostheses to restore edentulous mandibles is a highly effective, minimally invasive, and durable treatment. After ten years, the restorations showed 100% implant and prosthesis survival, stable peri-implant health with slight bone gain, and consistently high patient satisfaction without any technical complications [32]. This success is attributed to the FRC framework's stress-modulating properties [26], which enhance mechanical and biological compatibility [71], positioning it as a less invasive alternative to rigid metal-based systems. Additionally, FRCs supporting partial fixed dental prostheses (P-FDPs) on short implants achieved high survival and success rates

(95.9 vol. % and 89.8 vol. %, respectively) over nearly a decade [38, 98].

In Direct Restorations and Posts, FRCs significantly enhance the longevity of restored teeth [8]. The use of anatomically customized E-glass short fiber posts in weakened, endodontically treated premolars has been shown *in vitro* to improve mechanical properties and adaptability [33, 50, 81]. Furthermore, clinical trials have demonstrated that fiber-reinforced composite restorations in posterior Class II cavities achieved favorable outcomes in wear resistance, marginal integrity, and patient satisfaction over 18 months [9, 99]. Randomized clinical trials confirm that polyethylene fiber reinforcement in composites for endodontically treated teeth provides superior resistance to fracture and improved longevity compared to conventional composite restorations [8, 30, 63].

E. Oral and Maxillofacial Surgery

FRCs are increasingly being applied in oral implantology, particularly for bone anchorage and replacement as well as in major reconstructive procedures, including orbital floor repair [43], cranioplasty [100], and craniofacial bone reconstruction [37, 101]. The growing interest in these materials stems from their ability to address several biomechanical and clinical drawbacks associated with conventional metal implants. FRC-based devices exhibit an elastic modulus closer to that of natural bone [58], thereby reducing the risks of stress shielding and bone overloading. Moreover, they do not interfere with medical imaging modalities [43]. Structurally, the glass fibers provide the essential load-bearing capacity, while the gradual dissolution of bioactive glass particles simultaneously enhances bone integration and imparts antimicrobial properties to the implant. This unique combination of stress-modulating behavior and bioactivity

contributes to the improved mechanical performance and biological compatibility of FRCs in implant-based therapies [58, 26]

VII. CONCLUSION

FRCs have emerged as an innovative material in restorative dentistry, offering a combination of strength, esthetics, and versatility that can be tailored to specific clinical needs. Their unique properties allow for significantly improved durability, biocompatibility, and functionality compared to traditional restorative materials. Although some challenges remain regarding their long-term performance, continuous research and technological advancements are broadening the clinical applications of FRCs. These advancements include the incorporation of nanomaterials, bioactive components, and integration with CAD/CAM systems. FRCs also demonstrate potential beyond dentistry, including implantology and tissue engineering, highlighting their broader biomedical relevance. As innovations continue, FRCs are likely to play an increasingly significant role in providing effective and personalized restorative solutions, benefiting both patients and clinicians.

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**Investigation of Polymer/Metal
Applications for Enhanced
Performance in Biomedical Devices
and Biochemical Storage Systems**

Investigation of Polymer/Metal Applications for Enhanced Performance in Biomedical Devices and Biochemical Storage Systems

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Abstract

This research aims to provide a comprehensive overview of the fundamental concepts, modern techniques, and future challenges in bioprocess engineering, with an emphasis on its crucial role in developing effective and sustainable biological industrial solutions. Applications that contribute to resource sustainability are highlighted. This field utilizes biotechnology in various industrial applications, including food, blood samples and pharmaceuticals production, and modern Polymer science technologies such as advanced medical applications for a good connection of these materials with cells. The study reviews technical and regulatory challenges related to the medical development of modern technologies for example, stainless steel laser treatment and thermoplastic polymer improved. This publication, resulting from the research as a scientist in the United Kingdom, is directly linked to research in materials treatment, physics, and the applications of material polymer engineering. It encompasses

the application of thermoplastic polymer development, and laser treated stainless steel types 304 and 430, along with various metals commonly used for storing food, such as tomato sauces. This aspect of polymer science research primarily focuses on ensuring safe and healthy living conditions. The core objective of these studies is to guarantee the safety of food and human life. Therefore, plastic and thermoplastic polymers are used in a manner that safeguards our wellbeing. Importantly, these experimental studies have yielded a significant observation plastic and thermoplastic polymer containers for storing can lead to chemical degradation and contamination, which can rapidly seep into the consumables. This phenomenon poses health risks and raises important questions regarding environmental safety. The research is evaluated under established polymer analysis frameworks, including ISO 9000 standards, and supported by detailed experimental data, tables, and figures. The findings contribute to the broader field of environmental hazard science and offer insights into safer and more sustainable uses of materials in both medical and food-related applications.

Keywords: Polymer-metal applications, biomedical devices, stainless steel (SS) and thermoplastic polymers for storage system optimization, safety and security storage applications, polymer/metal degradation, organic molecule formation.

I. INTRODUCTION

The analysis examined the performance of chemical treatments applied to additively manufactured polymers, covering various types of polymers and Austenitic stainless steel 304. It also assessed how these treatments influenced the material properties of the polymers and 304 stainless steels. One treatment method of 304 stainless steels was a CO₂ Laser treatment. And various chemical treatments of

polymers were explored for their potential scientific and industrial applications. These applications around polymer type storage conditions on medicine and food safety, nutritional suitability, and contaminant food migration. This facet of polymer science research is primarily geared towards promoting safe and healthy living environments. Consequently, the use of plastic and polymer containers for storing food and beverages poses a risk of chemical degradation and contamination (Malle Adolf et al., 2025), potentially impacting the safety of consumables. Figure 1 illustrates alternatives for various food storage methods, while multiple studies have demonstrated the toxicity of plastic food packaging to both consumer health and the environment.

II. Biomaterials Review

A. Metallic Biomaterials

Metallic biomaterials are the most widely used category of biomaterials (Malle Adolf et al., 2025)). Their extensive application in medicine particularly in prosthetics and surgical procedures is largely due to the long service life of metal implants, which typically last around twenty years.

For metals to be suitable as biomaterials, they must primarily be non-toxic and bio tolerant. Their widespread use across various medical fields is attributed to their excellent electrical and thermal conductivity, as well as superior mechanical properties, including high strength under both static and dynamic loading conditions. These materials function as passive implants during bone fracture healing, are used in spinal fixation devices, and serve in numerous types of implants such as hip and knee replacements. However, the selection of metallic biomaterials for in vivo applications must be made with care, as corrosion can lead to serious complications. Corrosion may cause the spontaneous degradation of the implant material, resulting in

reduced mechanical integrity and the release of corrosion products that could negatively affect surrounding tissues and organs, as reported in various studies. Common metallic materials used in medical applications include 304 austenitic stainless steels, titanium and its alloys. Biomedical materials and polymer biomaterials (Figure 1). Owing to their unique and appealing properties, these materials can be combined to form bio-composite materials, which hold great promise for applications in medicine and tissue engineering.

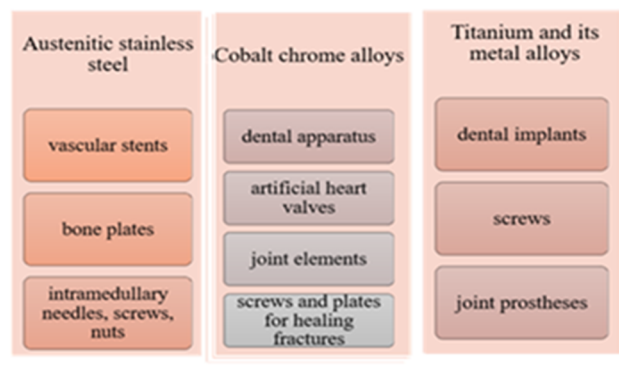


Figure 1. Selected metallic biomaterials use in medical [4].

B. Polymer Biomaterials

Polymers materials with a number of interesting features that make them desirable biomaterials in medicine and tissue engineering. These materials, figure 2, in addition to corrosion resistance in the environment of tissues and body fluids, show a very high bio-tolerance in the body [4].

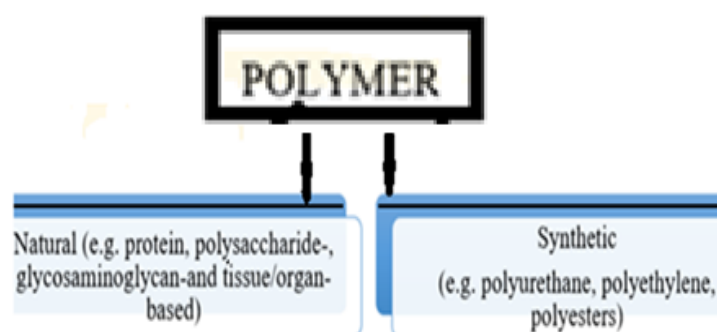


Figure 2. Classified of polymer biomaterials [4].

Polymers are a very interesting and constantly developing group of materials. Biodegradable polymers are widely used (Figure 3) in biomedical applications: tissue engineering and regenerative medicine [4–6]. However, these materials also have a number of disadvantages, including absorbing water and protein in the human body, and their surfaces are easily contaminated and difficult to sterilize. Properties of biomaterials based on natural and synthetic polymers as shows in figure 4.

Table 1. The samples composition and named

Sample	1% stabilizer	PP %	Graft
1-PP-Nor116		100	---
2- PP-APP 107		96	Polybond (pb)
3- PP-NOR-NH		91	Polybond
4- PP FR 107		91	Polybond
5- PP Amgard 107		91	Polybond
6- PP 3OB		96	Polybond
7- PP APP 3OB		92	--

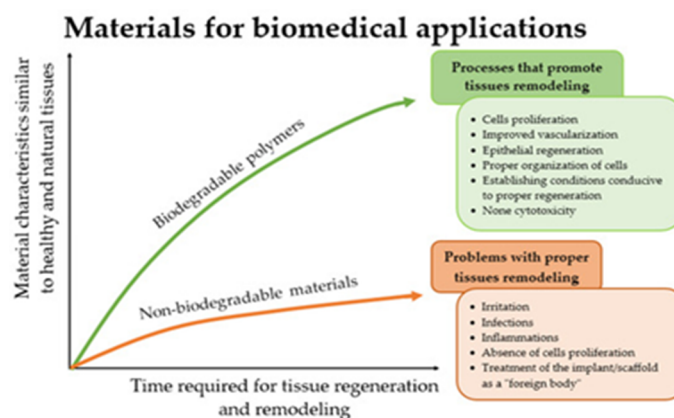


Figure 3. Diagram illustrating the advantages of using biodegradable materials compared to the use of solid materials in biomedical applications. Source: own compilation based on [7].

Polymeric materials may be divided into natural and synthetic. Although they differ in origin, their functions are similar. Due to their applications in biomedicine, these materials should be characterized by certain properties. The basic characteristics of these materials are shown in Figure 4.

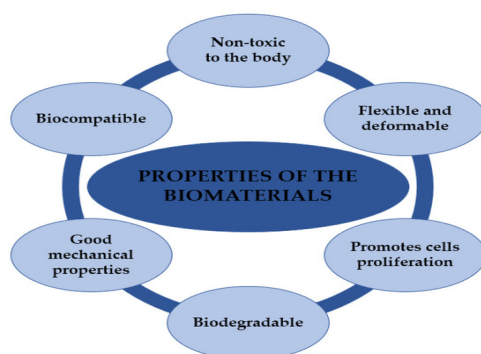


Figure 4. Properties of biomaterials based on natural and synthetic polymers.[Source: Jagoda Kurowiak, et al. 2023].

III. Materials treatment

Treatment was applied to assess the biodegradation effects of selected biomaterials on the human body.

A. Polymer chemical treatment

Under this part of this work introduces 7 various of polymer samples blended in a twin-screw extruder with different additive and 1% Stabiliser as recorded in table 1, to investigate polymers decomposition studying, physics, chemical properties and decomposition which affects the viscosity. XRD test either and DSC test for only PP polymer as shows in figure 5 and 6, Scanning Electron Microscopic (SEM) Figure 7 and its images have been used as seen as in figure 8.

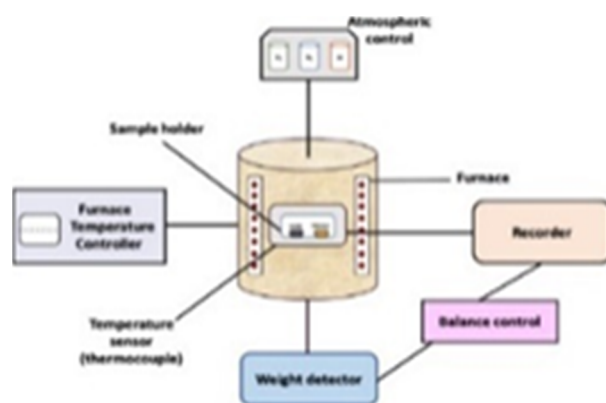


Figure 5. PP polymer DSC analysis. [From, Industrial Applications of Nanocrystals (IAN),2022].



Figure 6. The XRD technique



Figure 7. Scanning electron microscopic (SEM)

IV. Results and discussions

In the previous work for the same samples of polymers to verify the results and record a more precise outcome to draw the relationship between a different additives and decomposition behaviour. This work is extension of the first part which found the compatibilizer improves clay diffusion through the polymer changing the viscosity.

The advanced methods for examining the interior geometry, structure, and morphology of nanomaterials are discussed in this piece of writing, including Scanning electronic microscopy (SEM), and X-ray diffraction (XRD). Finally, the discussed the issues associated with nanomaterials in biomedical applications applied. PP Polymer properties have been examined with digital images using Scanning electron microscopic (SEM) as seen as in figure 8, shows a small

fraction of the polymer included, decomposition significantly reduces the molecular weight.



Figure 8. Shows PP polymer a small fraction of the polymer Included using Scanning electron microscopic (SEM).

The 7 polypropylene samples composition (wt %) and additives were blended with 1% Stabilizer as shown in table 1. X-ray diffraction (XRD) analysis technique curves as shows in Figure 9, uses for polymer samples for showing the effect of treatment additives on dispersion and diffusion of the metal which compound in polymer samples.

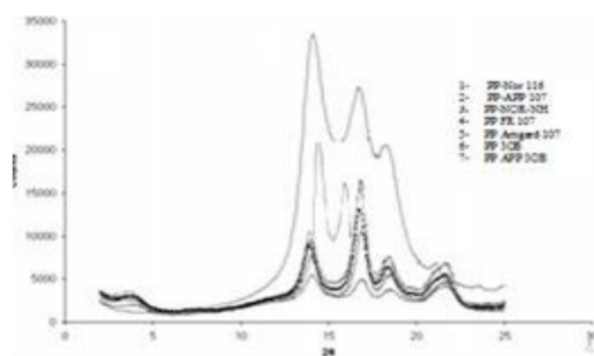


Figure 9. The XRD curves for polymer samples compounded additives

A. Corrosion studies

The etched structures were classified into the following types: step structure (steps only between grains, no ditches at grain boundaries), ditch structure (one or more grains completely surrounded by ditches) and Dual structure (some ditches at grain boundaries, but no single grain completely surrounded by ditches).

B. EPR electrochemical test

The good interpretation of the EPR test necessitates studying not only the evolutions of Q_r/Q_p values but also the evolutions of the separate Q_r and Q_p values. And current peak is also, an important parameter to

evaluate the performance of intergranular corrosion of stainless steel. Larger reaction peak and Q_r/Q_p corresponds to more sensitized specimen. From figure 10 EPR 304 S.S results of both samples are represented. These samples include initial received samples as well as the same samples after laser treatment in order to compare them. Table 2 shows E_{corr} shift negative after laser bending. The laser bended specimen presents a larger reactivation current than as received specimen. And it has larger Q_r/Q_p and I_r/I_p . It shows the former is prone to be attack by intergranular corrosion.

Table 2: Recorded EPR results of 304 S.S of both samples as received and the same sample after laser treatment to compare

Specimen	E_{corr}, V (vs.SCE)	Q_r (C/cm^2)	Q_p (C/cm^2)	I_r (mA)	I_p (mA)	Q_r/Q_p (%)	I_r/I_p (%)
As received	-0.4251	0.1091	4.0838	2.15	75.93	2.67	2.83
Laser-bent 304 S.S	-0.4379	0.3865	6.3772	4.46	88.19	6.06	5.06

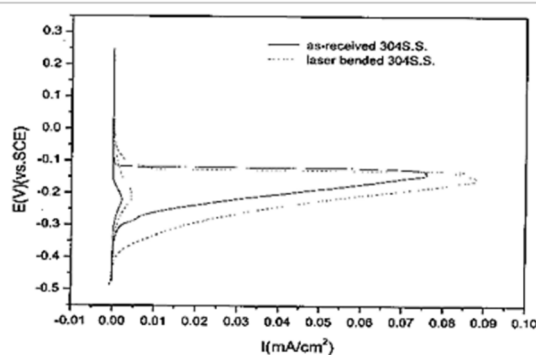


Figure 10. Shows EPR results of 304 S.S of both samples as received

C. Conclusions of Polymers treatment

Corresponding of these results as feedback from DSC, SEM, (DL-EPR) tests and XRD shows as well as recorded optimal distribution of some metal and crack and more are pointing on a pore connection of these materials with cells, in this case of using this type of material for the regeneration of bone tissue, the extremely important features are biocompatibility, biodegradation, appropriate. microstructure, electrolytic etching in oxalic acid and double-loop DL- EPR, for investigation electrochemical initial potential reactivation of 304 SS in biomedical materials applications.

This research highlights the significant impact of polymer degradation on food safety, security, and suitability under specified conditions. The study focused on the chemical degradation and contamination of various polymers, , the researchers are anticipated to provide guidance on ensuring the safety, security, and suitability medical application and storages. This poses a substantial risk to human health, especially when these containers are exposed to direct sunlight or reused multiple times.

V. Materials and laser treatment processing

Laser treatment by laser bending is a technique of treating sheet metal by thermal residual stresses generated by laser assisted heating without any externally applied mechanical forces. The advantages of laser assisted treatment over

Table 3: Chemical composition of the materials used in the experiments, wt. %

Alloy	C	Mn	P	S	Si	Cr	Ni	Fe
304	0.04	2.00	0.045	0.03	1.00	19.00	9.25	Bal.

conventional bending includes flexibility of non-contact processing, amenability to materials with diverse shape/geometry, and high precision/productivity. Up to now, most of previous work on laser bending was concentrated on study of bending angles/shapes with laser operating conditions, and modelling of the thermal process, however, no work has been reported on corrosion behaviour of the laser-bended components. Since the laser treatment process, it is believed that the process could not only alter microstructure, but also affect corrosion performances, such as intergranular corrosion, due to possible sensitisation caused by repeating laser scans.

The aim of the present work is to investigate corrosion performance also of laser treatment 304 austenitic steel with thicknesses of 2 mm and 1.5 mm, respectively, using a 2 kW CO₂ laser. After laser treatment, the laser treatment samples were characterised in terms of microstructural change within treatment zones consisting of melt-zone and heat-affected zone, using optical microscopy and scanning electron microscopy (SEM). Hardness profiles were obtained across the treatment zones. Corrosion performances of the laser treatment evaluated by means of electrolytic etching in oxalic acid and double-loop electrochemical initial potential reactivation (DL-EPR) tests. Laser bending is a thermal process, it is believed that the thermal process could not only alter microstructure, but also affect corrosion performances, due to possible sensitisation caused by repeating laser scans.

chemical compositions of ALSI 304 austenitic stainless steels used in this study are given in table 3. 304 SS alloy were received after solution treatment. Laser bending was carried out using a 2 kW CO₂ laser with Gaussian beam profile under Air shrouding environment to minimise oxidation. The dimension of both alloys is 100 mm x 30 mm with thickness of 2 mm and 1.5mm. One end of the sheet was clamped in a fixture to remain the length of the samples to be 90 mm. Laser beam is uniform across the width of the specimen (the x-direction) in

figure 11. The summary laser operating conditions are shown in table 4.

The chemical compositions of AISI 304 austenitic stainless steels used in this study are given in table 3. Alloy of 304 was received after solution treatment. Laser bending was carried out using a 2 kW CO₂ laser with Gaussian beam profile under Air shrouding environment to minimise oxidation. The dimension of this alloy is 100 mm x 30 mm with thickness of 2 mm and 1.5mm. One end of the sheet was clamped in a fixture to remain the length of the sheet to be 90 mm. Laser beam is uniform across the width of the specimen (the x-direction) in figure 11.

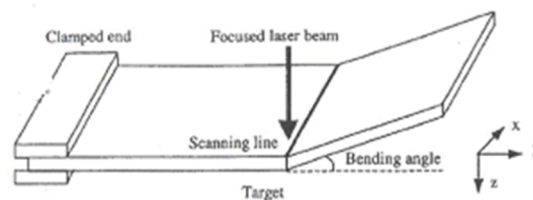


Figure 11. Schematic of laser bending process

Table 4: Summary of process parameter, the laser operating condition employed in laser treatment of AISI 304 stainless steel with Graphite coating:

Work piece thickness (mm)	Work piece width (cm)	Work piece length (cm)	Laser power (W)	Processing Velocity (m/min)	Passes Number (N)	Laser Spot diameter(D) (mm)

				)		
2	3	10	300-400	5-40	5-40	3

A. Materials characterization:

Microstructures of the alloys were examined after electro-etching in 10% oxalic acid at a current density of 1 A/cm^2 using optical microscopy and scanning electron microscopy (SEM). Microhardness cross the different regions of laser region, as seen as in figure 12, specimens was measured by a Vickers microhardness tester reported by Y. Shi *et al.* 2014). Further tested investigation determined by the DL-EPR in de-aerated $0.5\text{M H}_2\text{SO}_4 + 0.01\text{M KSCN}$ and scanning rate of 1.67 mV/s using Salortron 1280, potentiostat and a conventional three-electrode cell employing a Pt counter electrode and saturated calomel reference electrode (SCE). Freshly polished surfaces to 1200 grit with emery paper and 3 mm diamond paste in order to present a uniform surface roughness were immersed in the electrolyte for 30 min to determine the potential (E_{corr}). After establishing the E_{corr} , for 304 stainless steel, the specimen was polarised from the initial potential of $50 \text{ MV(vs.E}_{\text{corr}})$ in the cathodic region to a version potential (E_{rev}) of $+250\text{mV(vs.SCE)}$ in the passive region. As soon as this potential was reached, The scanning direction was reversed and potential was degreased to the cathodic region; in terms of degree of sensitisation, was characterised by the reactivation ratio, Q_r/Q_p (t, T), where Q_r (C/m^2) is the reactivation and Q_p (C/m^2) is the activation passivation surface charge density.

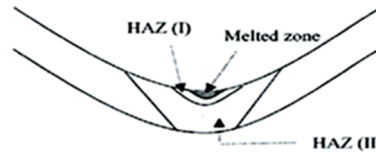


Figure 12. Schematic diagram of atypical bent zone

The SEM micrographs of laser treatment zone of Specimen 304 SS. Graphite coating at magnification (Inconel) X800 after exposure to etched by oxalic acid 10% are identified as recorded in figure 13.

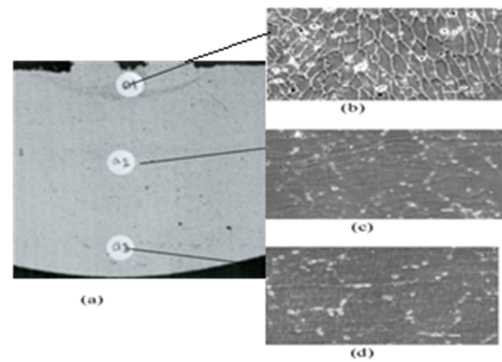


Figure 13. (a, b, c, d). SEM micrographs of laser treatment zone of Specimen 304 SS. Graphite coating at magnification (Inconel) X800 after exposure to etched by oxalic acid 10% are identified as (a): general appearance-cross section, (b): melted zone, and (c): HAZ (I) and (d): HAZ (II).

B. Conclusions of 304 SS laser treatment

In this work, laser treatment of 304 austenitic stainless steel only has been investigated in terms of microstructure and corrosion performance within bent-zone and HAZs. The following conclusions are drawn:

The microstructure of the treatment zone consisted of melt zone with significantly refined dendritic structure and followed by HAZ (I) with coarsened grains and then by HAZ (II) with pronounced grain elongation.

Conclusion for biomedical materials and their medical application

This phenomenon accounts for their currently limited clinical application (11). Such undesirable reactions frequently disrupt the healing cascade, inducing severe patient discomfort, pronounced inflammation, and tissue degradation, which may culminate in graft or implant rejection. Consequently, a central objective within the biomaterials research community is the rational design of multifunctional materials endowed with attributes such as biodegradability, the ability to control drug release [or sensitivity to stimuli, while addressing ways to overcome immune barriers, inflammation, and endotoxin contamination (11). The advancement of novel biomaterials, the rising demand for medical implants, and the escalating prevalence of cardiovascular disorders collectively contribute to increased financial allocations within the healthcare policies of numerous nations globally.

C. Conclusion for biomedical materials and their storage applications

Overall, this research underscores the need for ongoing scrutiny and improvement of food packaging materials to safeguard public health. Future work should focus on developing more resilient polymers and enhancing regulatory frameworks to address emerging risks. Recommendations will include strategies for safer food storage practices, particularly regarding the use of polymers, to ensure the continued safety, security, and suitability of food packaging materials. The plastics storage of blood, Pharmaceuticals and food, are usually made up of low-density polyethylene (LDPE) that serve as the environmental problems. The weight loss of the treated piece of

plastics (LDPE), respectively. Polyethylene pieces were characterized by analysis before and after biodegradation, that as a resulting of the isolated bacterial strains have a good potential to degrade LDPE biodegradation, therefore, the weight loss easy occurs in piece of plastics (LDPE), and it was calculated by the following formula.

$$\text{Weight loss (\%)} = \frac{\text{Initial weight} - \text{Final weigh}}{\text{Initial weigh}} \times 100 \quad (1)$$

Following by Drow the specific curve corresponding the mass loos the time as mentioned in figure 14.

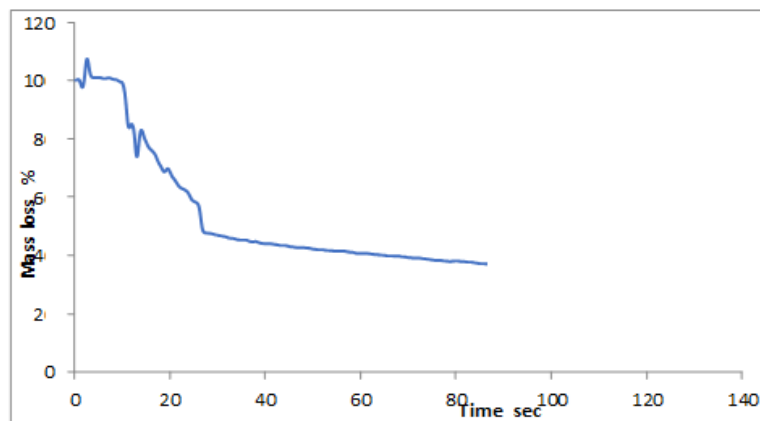


Figure 14. Shows mass loss with time at the degradation of polymer PP sample recorded in table 1

Studies and research of plastic and polymer containers for storing can lead to chemical degradation and contamination, including ISO 9000 standards, and supported by detailed experimental data, tables, and figures. Avoid degradation of normal substances and are proved dangerous to human, animals and the ecosystem by Windsor et al. 2019. Preferably, polymers with lower degradation rates, such as PLA, should be chosen over others. Additionally, discouraging the repeated

use of PET bottles, especially for acidic or coloured beverages, is advisable to mitigate risks.

Several research W. Sun, F.G. Wu, 2018, A. Murali, et al, 2021, N.H. Solangi, et al. 2023 and Nadeem Hussain Solangi, et al, 2023 works achieved for against bacteria using 2D materials. Other 2D nanomaterials for biomedical applications Through the production of superoxide radicals or directly through the oxygenation of bacterial cellular receptors by nanoparticles, transition metal dichalcogenides (TMDs) development of bacteria (12).

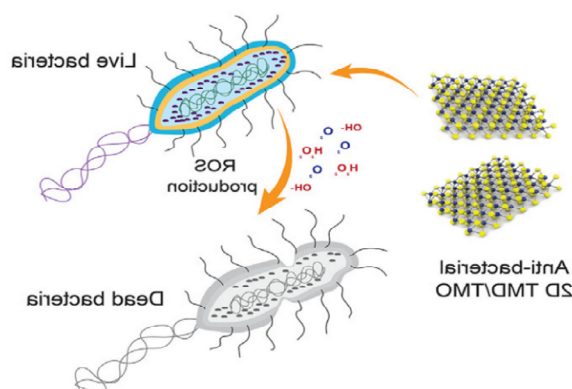


Figure 15. The bacterial cell dies due to a rise in ROS generation, an exploded diagram of how TMDs and TMOs work against bacteria [13].

VI. Future studies and challenges

A. Future studies follow present studies

Currently, numerous studies are being carried out on the use of polymer–ceramic composites as a material in the regenerative

medicine of bone tissue. This approach allows for a more accurate reconstruction of the entire bone structure. Polymer matrices combined with bio-ceramics or bioactive glasses allow imitation of the organic and mineral phase found in the bone, which enables better regeneration of the damaged tissue or organ. Depending on the application, polymer–ceramic composites must have specific characteristics, by Malle Adolf et al. 2025 research.

Commonly used additives in plastics that can be released into environment during the production, application and disposal of plastics materials, both the plastics behaviour such as the fraction and its degradation products pose health risk to the environment and human health. A few studies by Nadeem et al., 2021 and Malle Adolf et. al., 2025, demonstrates that a simple constructed microbial consortium based on step-by step biodegradation principal can fast and efficiently biodegrade providing a feasible industrial application and environmental applications for construction microbial groups. The constructed microbial consortium, whether consisting of two or three bacterial strains, achieved 100 %. Additionally, studies have demonstrated that biodegradable metals may possess superior mechanical properties compared to biodegradable polymers. Examples of such materials include porous magnesium or iron alloys. Recent research has focused on incorporating magnesium into the polymer matrix. The study showed that magnesium would provide higher mechanical strength and fracture toughness, and the polymer would prevent premature degradation of the composite [16], these materials exhibit mechanical properties similar to those of human bone.

B. Perspectives for Further Research follows present studies: Challenges and Constraints

The potential of natural and synthetic polymers in biomedical applications is very high. A lot of research has already been

performed, providing us with valuable information on the structure, properties and potential functions of polymers. Scientists around the world are successfully conducting research into the applicability of polymeric materials. Attempts are being made to produce hybrid polymer materials and to characterize them using innovative equipment to image them and even identify their internal structures. Another important area of research is that aimed at developing polymer coatings for non-degradable materials. Such coatings are intended to increase bio tolerance and acceptance at the implantation site. Surface modifications of medical devices based on biodegradable polymers may contribute to greater effectiveness in the treatment of various diseases (urological, circulatory system and difficult-to-heal wounds). In order to safely apply the proposed solutions in medical areas, it is crucial to conduct intensive research into clinical requirements [17]. Biodegradable polymer materials used in medicine, depending on the place of implantation and purpose, will be exposed to various external stimuli: pressure, flow, temperature, variable stresses and strains and electric fields. The materials used must be resistant to these stimuli and should adapt to changing conditions. It is these variables that seem to be the most challenging to understand and solve. There is no doubt that, in recent years, there has been explosive growth, success and breakthrough in the manufacture of multifunctional biodegradable polymer materials. Further research should concern chemical modifications and the creation of hybrid polymer biocomposites that are capable of imitating and regenerating bone and/or soft tissues [18].

The achievements accounted for here, and their scales, are impressive. The importance of ongoing development of these materials for medicine and the treatment of patients is evident. Interdisciplinary research combining tissue engineering, regenerative medicine and biomaterials science is opening new avenues for future research. Despite the many successes that have already been achieved, many

questions continue to arise; these will continue into the future, revealing yet undiscovered and potentially even surprising problems and challenges. Intensive research into enhancing the biocompatibility of biomaterials and their proper biological adaptation to the tissue environment must continue. Consideration should be given to the question of improving the body's response to implants and reducing inflammatory reactions.

C. Perspectives for Further Nanomaterials

Research: Challenges and Constraints

Biomedical Nanomaterials materials' internal structure, sizes, and shapes enable various applications in biomedical science, energy production, batteries and medical application such as Carbone Nano Tube(NCT) via antibiotic medicines applications. Nanomaterials are effective materials for drug delivery to treat the affected part of the body against the virus because their structure matches various affected parts. So, they perform better to kill or limit the growth of bacteria, advantages and disadvantages properties of nanomaterials such as polymers and metal (304 SS) as a height of this study. Nanomaterials are magical substances for biomedical applications (figure 16) because of their characteristics in the present time. Nanomaterials are widely utilized in biomedical sectors such as antibacterial activity, cell culture, recovering medicine, drug delivery and tissue engineering study by N.H. Solangi, et al., (2023).



Figure 16. Various biomedical applications of nanomaterials

Nanotechnology is the branch of engineering in which scientists study the structure and behavior during the targeted drug delivery and geometry of materials via various advanced characterization techniques. In nanotechnology, scientists work on those materials that size are 1-100 nm with unique morphology, geometry, and shapes (15 and 19).

VII. RECOMINDATION

Biomaterials are brittle and do not satisfy the mechanical characteristics of bone. Synthetic Polymeric Materials in Modern Medical Applications, Poly (-caprolactone) (PCL), a type of synthetic polyester derived from hydroxyalkanoic acids, has received approval for clinical use. Presenting biologically active factors on the surfaces of synthetic polymers is the most effective method for stimulating desired interactions between cells and materials by Nadeem et al., (2021).

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**Development of an AI-Based Non-Invasive
Pre-Screening and Clinical Decision
Support System for Coronary Artery
Disease**

Development of an AI-Based Non-Invasive Pre-Screening and Clinical Decision Support System for Coronary Artery Disease

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Abstract

Cardiac catheterization remains the clinical gold standard for diagnosing coronary artery disease (CAD), allowing direct assessment of coronary artery status and enabling interventional procedures such as angioplasty and stenting. However, as an invasive and costly procedure, it is associated with potential complications including bleeding, contrast-related reactions, vascular injury, and other procedure-related risks. These limitations highlight the need for

supportive non-invasive approaches that can assist in early patient evaluation and clinical triage.

This study proposes the development of an artificial intelligence (AI)-based non-invasive pre-screening and clinical decision-support system for the early identification of patients at risk of coronary artery disease. The proposed model is designed to assist clinicians in evaluating the likelihood of coronary artery stenosis using primary clinical data, including patient symptoms, electrocardiogram (ECG) findings, blood test results, lifestyle-related factors, and medical history.

The system is implemented using MATLAB and employs machine learning algorithms to identify patterns and predictive markers associated with CAD. Rather than replacing cardiac catheterization, the proposed model serves as a supportive tool to enhance early risk stratification, optimize patient triage, and potentially reduce unnecessary invasive procedures.

By integrating artificial intelligence into clinical assessment, this study aims to improve diagnostic support, facilitate timely medical decision-making, and promote safer and more efficient patient management.

Keywords: Coronary Artery Stenosis--Non-Invasive Diagnosis--Cardiac Disease Detection--Neural Networks for Cardiology --Automated ST-T Analysis--Intelligent Cardiac Care System--ECG Machine Learning Algorithms—Explainable

I. INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality globally, accounting for an estimated 17.9 million deaths annually and representing approximately 32% of all global deaths. Among

cardiovascular disorders, coronary artery disease (CAD) stands as the most prevalent and lethal manifestation, responsible for significant healthcare expenditure and profound deterioration in patients' quality of life. The substantial clinical and economic burden imposed by CAD has intensified the imperative for accurate, timely, and accessible diagnostic methodologies that can facilitate early detection and guide appropriate therapeutic interventions.

The diagnosis of coronary artery disease traditionally relies on a hierarchical approach beginning with clinical assessment, risk stratification, and non-invasive testing, culminating—when indicated—in invasive coronary angiography (ICA) with physiological assessment. Invasive coronary angiography, coupled with fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) measurements, constitutes the established gold standard for evaluating the anatomical and hemodynamic significance of coronary stenoses [1, 2]. This invasive approach enables direct visualization of coronary anatomy, precise quantification of stenosis severity, and simultaneous therapeutic intervention through percutaneous coronary intervention (PCI) when appropriate. However, despite its diagnostic precision, invasive catheterization carries inherent procedural risks including vascular complications, contrast-induced nephropathy, radiation exposure, and rare but serious adverse events such as coronary dissection or myocardial infarction. Furthermore, the procedure demands specialized catheterization laboratories, highly trained personnel, and substantial financial resources, limiting its accessibility in resource-constrained healthcare settings and rendering it impractical as a first-line screening tool for the broader at-risk population.

Consequently, contemporary cardiology practice has increasingly emphasized non-invasive diagnostic modalities for initial CAD

assessment and risk stratification. Conventional non-invasive techniques include resting and exercise electrocardiography (ECG), stress testing with imaging (echocardiography, myocardial perfusion scintigraphy), cardiac magnetic resonance imaging (MRI), and coronary computed tomography angiography (CCTA). While CCTA has demonstrated excellent negative predictive value for excluding obstructive CAD, its ability to determine the functional significance of intermediate stenoses remains limited, as anatomical stenosis severity does not consistently correlate with hemodynamic relevance [3]. Similarly, standard ECG exhibits limited sensitivity for detecting functionally significant coronary stenoses in many patient cohorts, and stress testing modalities demonstrate variable accuracy with substantial operator and reader dependence [4, 5]. These diagnostic limitations underscore a persistent clinical gap: the need for accurate, non-invasive methods capable of identifying hemodynamically significant CAD while avoiding the risks, costs, and resource demands of routine invasive angiography.

The advent of artificial intelligence (AI) and machine learning technologies has ushered in a transformative era in cardiovascular diagnostics, offering unprecedented capabilities for analyzing complex, multidimensional medical data with speed and accuracy that often surpass traditional interpretative methods. Recent advances in deep learning architectures, particularly convolutional neural networks and ensemble learning models, have enabled the development of sophisticated AI algorithms capable of extracting subtle diagnostic patterns from diverse data sources including electrocardiograms, echocardiographic images, photoplethysmography signals, and computed tomography datasets [6, 7]. Emerging AI-driven diagnostic tools now span multiple domains: physiological estimation algorithms that derive fractional flow reserve from CT angiography (CT-FFR) or invasive angiography images (angio-FFR), automated coronary

stenosis quantification systems, AI-enhanced interpretation of myocardial perfusion imaging, and signal-based screening tools utilizing ECG or peripheral pulse waveforms [1, 2, 8].

Clinical validation studies have demonstrated promising diagnostic performance for these AI-enabled non-invasive approaches. For instance, machine learning-derived CT-FFR systems have achieved sensitivities ranging from 76.8% to 91% and specificities between 94.3% and 95% when validated against invasive FFR, with area under the curve (AUC) values consistently exceeding 0.90 in multiple studies [2, 9, 10]. Similarly, deep learning algorithms applied to coronary CT angiography have shown diagnostic accuracy rates of approximately 87-94% for detecting hemodynamically significant stenoses, with calculation times reduced to under one minute compared to conventional manual analysis requiring several minutes [11, 12]. Novel point-of-care systems utilizing photoplethysmography signals processed through machine learning algorithms have demonstrated AUC values of 0.80 with negative predictive values reaching 0.99 in low-prevalence populations, suggesting potential utility as rapid screening tools [13]. Furthermore, AI-augmented coronary stenosis quantification on CCTA has demonstrated improved concordance with invasive quantitative coronary angiography compared to human readers, particularly benefiting less experienced interpreters [14].

Beyond diagnostic accuracy, AI integration offers several compelling advantages that address fundamental limitations of current practice. First, AI algorithms substantially accelerate diagnostic workflows, with processing times reduced from hundreds of seconds for manual analysis to mere seconds for automated AI interpretation—a critical advantage in time-sensitive clinical scenarios [12, 15]. Second, retrospective analyses and modeling studies suggest that deploying

AI-derived CT-FFR as a gatekeeper prior to invasive angiography could reduce unnecessary ICA procedures by approximately 54.5%, potentially translating to substantial cost savings and reduced patient exposure to procedural risks [16]. Third, automated AI systems may enhance diagnostic consistency and reduce inter-observer variability, particularly in settings with limited access to subspecialty expertise [14]. Fourth, by enabling accurate non-invasive assessment of coronary physiology, AI tools may facilitate earlier risk stratification and expand diagnostic access to populations currently underserved by invasive catheterization facilities.

Despite these promising developments, significant challenges and knowledge gaps persist before AI can be widely adopted as a reliable alternative to invasive catheterization in clinical practice. Current limitations include concerns regarding algorithm robustness and generalizability across diverse patient populations, scanner platforms, and healthcare settings [17]. Performance of AI-CCTA systems may be adversely affected by specific anatomical factors such as extensive coronary calcification, long lesion length, or complex plaque morphology, necessitating manual review or adjustment in certain cases [18]. Moreover, while numerous single-center and retrospective validation studies have reported high diagnostic accuracy, large-scale prospective multicenter trials with hard clinical outcome endpoints remain limited [3, 16]. The evidence base would benefit from rigorous evaluation across diverse demographic subgroups—including underrepresented populations defined by sex, race, ethnicity, and comorbidity profiles—to ensure equitable diagnostic performance. Additionally, comprehensive health economic analyses demonstrating cost-effectiveness in real-world healthcare systems, alongside implementation science research addressing workflow integration, regulatory approval pathways, and clinician acceptance, are essential prerequisites for widespread clinical adoption [17].

Ethical and regulatory considerations add further complexity to AI deployment in cardiovascular diagnostics. Issues of data privacy, algorithmic transparency, liability frameworks, and the need for continuous post-market surveillance to detect performance drift must be systematically addressed. The integration of explainable AI techniques that provide clinically interpretable rationales for diagnostic predictions may enhance physician trust and facilitate appropriate clinical decision-making [15]. Furthermore, the substantial digital infrastructure requirements—including high-quality imaging equipment, robust data management systems, and computational resources—may pose barriers to implementation in resource-limited settings, potentially exacerbating existing healthcare disparities.

Given these considerations, there exists a compelling rationale for rigorous investigation into the role of artificial intelligence as a non-invasive diagnostic alternative to traditional cardiac catheterization. While current evidence demonstrates promising diagnostic performance and potential clinical benefits, critical questions remain regarding optimal clinical integration strategies, real-world effectiveness across diverse populations and healthcare contexts, and long-term impact on patient outcomes and healthcare resource utilization. This research seeks to comprehensively evaluate the current state of AI-enabled non-invasive cardiovascular diagnostics, critically appraise the evidence supporting their clinical validity, identify remaining knowledge gaps and implementation barriers, and propose evidence-based recommendations for their judicious integration into contemporary cardiology practice. By synthesizing findings from recent clinical validation studies, examining performance characteristics across different AI modalities and patient populations, and analyzing the practical, ethical, and economic dimensions of AI deployment, this work aims to advance

understanding of how artificial intelligence can enhance diagnostic accuracy, reduce procedural risks, improve healthcare efficiency, and ultimately support clinicians in delivering safer, more effective, and more equitable cardiovascular care.

II. METHODOLOGY

A. Research Design and Framework

This study employs a quantitative, predictive modeling approach to develop an intelligent simulation model for non-invasive CAD diagnosis. The research framework follows a systematic pipeline consisting of data acquisition, preprocessing, feature engineering, model development, optimization, and validation phases. The methodology is designed to ensure reproducibility, clinical relevance, and statistical rigor.

1. Research Objectives

The primary objective is to develop and validate machine learning models capable of accurately predicting the presence and severity of coronary artery disease using non-invasive clinical parameters. Secondary objectives include:

1. Identifying the most diagnostically relevant clinical features through systematic feature selection
2. Comparing the performance of multiple ML algorithms to determine optimal model architecture
3. Implementing hyperparameter optimization to maximize predictive accuracy
4. Validating model performance using clinically relevant metrics
5. Ensuring model interpretability for clinical decision support

B. Data Collection and Dataset Description

1. Data Source

The study utilizes the UCI Heart Disease Dataset, a widely recognized benchmark dataset in cardiovascular research [9, 10]. This dataset aggregates clinical data from four major medical institutions:

- Cleveland Clinic Foundation (Cleveland, Ohio, USA)
- Hungarian Institute of Cardiology (Budapest, Hungary)
- V.A. Medical Center (Long Beach, California, USA)
- University Hospital (Zurich, Switzerland)

2. Dataset Characteristics

The dataset comprises 1,025 patient records with 14 clinical attributes. Each record represents a unique patient encounter with comprehensive clinical measurements. The target variable indicates the presence and severity of coronary artery disease, classified on a scale from 0 (no disease) to 4 (severe disease).

3. Clinical Variables and Features

The dataset includes the following clinical parameters:

- Demographic Features:
 - 1) Age: Patient age in years (continuous variable, range: 29-77 years)
 - 2) Sex: Biological sex (binary: 1 = male, 0 = female)
- Clinical Examination Features:
 - a. Chest Pain Type (cp): Categorical variable with four levels:
 - i. Type 1: Typical angina
 - ii. Type 2: Atypical angina
 - iii. Type 3: Non-anginal pain
 - iv. Type 4: Asymptomatic

- b. Resting Blood Pressure (trestbps): Measured in mm Hg upon hospital admission
- c. Fasting Blood Sugar (fbs): Binary indicator (1 if > 120 mg/dl, 0 otherwise)
- d. Resting Electrocardiographic Results (restecg): Categorical with three levels:
 - i. 0: Normal
 - ii. 1: ST-T wave abnormality
 - e. 2: Left ventricular hypertrophy
- **Exercise Test Features:**
 - 1) Maximum Heart Rate Achieved (thalach): Peak heart rate during exercise testing
 - 2) Exercise-Induced Angina (exang): Binary indicator (1 = yes, 0 = no)
 - 3) ST Depression Induced by Exercise (oldpeak): Continuous measure of ST segment depression
- Slope of Peak Exercise ST Segment (slope): Categorical variable:
 - 1) 1: Upsloping
 - 2) 2: Flat
 - 3) 3: Downsloping
- Laboratory and Diagnostic Features:
 - 1) Serum Cholesterol (chol): Total cholesterol in mg/dl
 - 2) Number of Major Vessels Colored by Fluoroscopy (ca): Range 0-3
- Thalassemia (thal): Categorical variable:
 - 1) 3: Normal
 - 2) 6: Fixed defect
 - 3) 7: Reversible defect

- 4) Target Variable: Diagnosis (num): CAD severity classification (0-4, where 0 = no disease)

C. Ethical Considerations

The UCI Heart Disease Dataset is publicly available and de-identified, complying with ethical standards for health data research [19, 20]. All patient identifiers have been removed to ensure privacy and confidentiality. The use of this dataset for research purposes aligns with established guidelines for secondary data analysis in medical research.

A. Data Preprocessing Pipeline

a. Missing Data Analysis and Imputation

The initial data quality assessment revealed missing values across several features. Missing data patterns were analyzed using the following approach:

1. Missing Data Quantification: Calculated the percentage of missing values for each feature
2. Missing Data Mechanism Assessment: Evaluated whether data was missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR)
3. Imputation Strategy:
 - For continuous variables with < 5% missing data: Mean imputation
 - For categorical variables: Mode imputation
 - For variables with > 30% missing data: Considered for exclusion or advanced imputation techniques (K-Nearest Neighbors imputation)
 -

b. Outlier Detection and Treatment

Outliers were identified and handled using the Interquartile Range (IQR) method [11, 12], a robust statistical technique that minimizes the influence of extreme values:

IQR Method:

$Q1 = 25\text{th percentile}$

$Q3 = 75\text{th percentile}$

$IQR = Q3 - Q1$

$\text{Lower Bound} = Q1 - 1.5 \times IQR$

$\text{Upper Bound} = Q3 + 1.5 \times IQR$

Values falling outside the [Lower Bound, Upper Bound] range were classified as outliers. Treatment strategies included:

1. Clinical Validation: Outliers were first assessed for clinical plausibility
2. Winsorization: Extreme values were capped at the upper/lower bounds for clinically valid outliers
3. Removal: Physiologically impossible values were excluded from analysis

c. Data Normalization and Scaling

To ensure optimal model performance and prevent features with larger scales from dominating the learning process, StandardScaler normalization was applied [13, 14]. This technique transforms features to have zero mean and unit variance:

$$z = (x - \mu) / \sigma$$

Where:

- x = original feature value
- μ = mean of the feature
- σ = standard deviation of the feature
- z = standardized value

StandardScaler was chosen over alternative normalization methods (MinMaxScaler, RobustScaler) because:

- It preserves the shape of the original distribution
- It is less sensitive to outliers after outlier treatment
- It performs well with algorithms that assume normally distributed features (e.g., Logistic Regression, Neural Networks)

d. Target Variable Transformation

The original target variable (num) with five classes (0-4) was transformed into a binary classification problem:

- Class 0: No CAD (original value = 0)
- Class 1: Presence of CAD (original values = 1, 2, 3, 4)

This transformation was implemented to:

1. Align with the primary clinical decision point (presence vs. absence of disease)
2. Address class imbalance issues in the original multi-class distribution
3. Improve model performance and clinical interpretability

E. Feature Engineering and Selection

a. Feature Selection Rationale

Feature selection is critical for developing parsimonious, interpretable, and generalizable models. Irrelevant or redundant features can lead to overfitting, increased computational complexity, and reduced model interpretability.

b. Mutual Information-Based Feature Selection

Mutual Information (MI) was employed as the primary feature selection criterion [15, 16]. MI measures the dependency between each feature and the target variable, quantifying how much information about the target is gained by observing a feature.

Mutual Information Formula:

$$I(X; Y) = \sum \sum p(x,y) \log(p(x,y) / (p(x)p(y)))$$

Where:

- X = feature variable
- Y = target variable
- $p(x,y)$ = joint probability distribution
- $p(x), p(y)$ = marginal probability distributions

Feature Selection Process:

1. Calculate MI score for each feature
2. Rank features by MI score in descending order
3. Select top N features based on:
 - MI score threshold (e.g., $MI > 0.05$)
 - Cumulative information criterion (e.g., top features explaining 95% of total MI)

- Domain knowledge and clinical relevance

c. Selected Features

Based on MI analysis and clinical validation, the following features were selected for model development:

High-Importance Features ($MI > 0.15$):

- Chest pain type (cp)
- Number of major vessels colored by fluoroscopy (ca)
- Thalassemia status (thal)
- ST depression induced by exercise (oldpeak)

Moderate-Importance Features ($0.05 < MI < 0.15$):

- Maximum heart rate achieved (thalach)
- Exercise-induced angina (exang)
- Slope of peak exercise ST segment (slope)
- Age
- Sex

Supporting Features ($MI > 0.05$):

- Resting blood pressure (trestbps)
- Serum cholesterol (chol)
- Fasting blood sugar (fbs)
- Resting ECG results (restecg)

F. Machine Learning Model Development

a. Algorithm Selection

Six machine learning algorithms were selected based on their proven efficacy in medical classification tasks and diverse learning paradigms:

1. Logistic Regression (LR): Baseline linear model for binary classification
2. K-Nearest Neighbors (KNN): Instance-based learning algorithm
3. Support Vector Machine (SVM): Maximum margin classifier with kernel trick capability
4. Decision Tree (DT): Rule-based, interpretable tree structure
5. Random Forest (RF): Ensemble of decision trees with bagging
6. Gradient Boosting (GB): Sequential ensemble learning with boosting

b. Model Training Strategy

Train-Test Split:

- Training Set: 80% of data (820 samples)
- Test Set: 20% of data (205 samples)
- Stratified sampling to maintain class distribution
- Cross-Validation:
- 10-fold stratified cross-validation for robust performance estimation
- Repeated cross-validation (5 repetitions) for stability assessment

c. Hyperparameter Optimization

Hyperparameter tuning was performed using Grid Search with cross-validation to identify optimal model configurations:

Logistic Regression:

- Regularization parameter (C): [0.001, 0.01, 0.1, 1, 10, 100]
- Penalty: ['l1', 'l2']
- Solver: ['liblinear', 'saga']

- K-Nearest Neighbors:
- Number of neighbors (k): [3, 5, 7, 9, 11, 15, 21]
- Distance metric: ['euclidean', 'manhattan', 'minkowski']
- Weights: ['uniform', 'distance']
- Support Vector Machine:
- Kernel: ['linear', 'rbf', 'poly']
- Regularization (C): [0.1, 1, 10, 100]
- Gamma: ['scale', 'auto', 0.001, 0.01, 0.1]
- Decision Tree:
- Maximum depth: [3, 5, 7, 10, 15, 20, None]
- Minimum samples split: [2, 5, 10, 20]
- Minimum samples leaf: [1, 2, 4, 8]
- Criterion: ['gini', 'entropy']
- Random Forest:
- Number of estimators: [50, 100, 200, 300, 500]
- Maximum depth: [10, 20, 30, None]
- Minimum samples split: [2, 5, 10]
- Minimum samples leaf: [1, 2, 4]
- Gradient Boosting:
- Number of estimators: [50, 100, 200, 300]
- Learning rate: [0.01, 0.05, 0.1, 0.2]
- Maximum depth: [3, 5, 7, 9]
- Subsample: [0.8, 0.9, 1.0]

G. Model Evaluation Framework

a. Performance Metrics

Model performance was assessed using multiple metrics to provide comprehensive evaluation [17, 18]:

Primary Metrics:

1. Accuracy: Overall correctness of predictions
2. $\text{Accuracy} = (\text{TP} + \text{TN}) / (\text{TP} + \text{TN} + \text{FP} + \text{FN})$
3. Precision: Proportion of positive predictions that are correct
4. $\text{Precision} = \text{TP} / (\text{TP} + \text{FP})$
5. Recall (Sensitivity): Proportion of actual positives correctly identified
6. $\text{Recall} = \text{TP} / (\text{TP} + \text{FN})$
7. F1-Score: Harmonic mean of precision and recall
8. $\text{F1} = 2 \times (\text{Precision} \times \text{Recall}) / (\text{Precision} + \text{Recall})$
9. Specificity: Proportion of actual negatives correctly identified
10. $\text{Specificity} = \text{TN} / (\text{TN} + \text{FP})$

Secondary Metrics:

1. Area Under ROC Curve (AUC-ROC): Measure of model's ability to discriminate between classes
2. Area Under Precision-Recall Curve (AUC-PR): Performance measure for imbalanced datasets
3. Matthews Correlation Coefficient (MCC): Balanced measure accounting for all confusion matrix elements

Where:

- TP = True Positives
- TN = True Negatives
- FP = False Positives
- FN = False Negatives

b. Clinical Performance Criteria

Given the clinical context, the following performance criteria were prioritized:

1. High Sensitivity (Recall): Minimizing false negatives is critical to avoid missing CAD cases
2. Acceptable Specificity: Reducing false positives to minimize unnecessary invasive procedures
3. Balanced F1-Score: Ensuring overall diagnostic reliability
4. High AUC-ROC: Demonstrating strong discriminative ability across decision thresholds

Target performance thresholds:

- Sensitivity $\geq 85\%$
- Specificity $\geq 80\%$
- F1-Score ≥ 0.85
- AUC-ROC ≥ 0.90

Statistical Validation

Confidence Intervals:

- 95% confidence intervals calculated for all performance metrics using bootstrap resampling (1,000 iterations)

Statistical Significance Testing:

1. McNemar's test for comparing paired classifiers
2. DeLong's test for comparing AUC-ROC values
3. Significance level: $\alpha = 0.05$

Model Stability Assessment:

1. Performance variance across cross-validation folds

2. Learning curves to assess overfitting/underfitting
3. Calibration plots to evaluate probability predictions

H. Model Interpretability and Clinical Validation

a. Feature Importance Analysis

Feature importance was calculated using multiple methods:

1. Permutation Importance: Measuring performance decrease when feature values are randomly shuffled
2. SHAP (SHapley Additive exPlanations): Unified approach to explain model predictions
3. Partial Dependence Plots: Visualizing the marginal effect of features on predictions

b. Clinical Decision Threshold Optimization

The classification threshold (default = 0.5) was optimized to maximize clinical utility:

1. ROC Curve Analysis: Identifying optimal threshold balancing sensitivity and specificity
2. Precision-Recall Curve: Evaluating threshold impact on precision-recall trade-off
3. Cost-Benefit Analysis: Incorporating clinical costs of false positives and false negatives

c. Model Deployment Considerations

For clinical implementation, the following factors were considered:

1. Computational Efficiency: Inference time < 1 second per patient
2. Interpretability: Ability to explain predictions to clinicians
3. Robustness: Performance stability across different patient subgroups

4. Calibration: Alignment between predicted probabilities and observed outcomes
5. Integration: Compatibility with electronic health record (EHR) systems

I. Software and Computational Environment

Programming Language: MATLAB+

Core Libraries:

- Data Manipulation: pandas 1.5+, numpy 1.23+
- Machine Learning: scikit-learn 1.2+
- Visualization: matplotlib 3.6+, seaborn 0.12+
- Statistical Analysis: scipy 1.10+, statsmodels 0.14+
- Model Interpretation: SHAP 0.41+

Hardware Specifications:

- Processor: Intel Core i7 or equivalent
- RAM: 16 GB minimum
- Storage: SSD with 100 GB available space

Version Control and Reproducibility:

- Git for version control
- Random seed fixed (seed = 42) for reproducibility
- Environment management using conda/virtualenv

III.RESULTS

Table 1: Model Performance Comparison On Test Set (N=205)

Model	Accuracy (%)	Precision (%)	Recall/Sensitivity (%)	F1-Score (%)	Specificity (%)	AUC-ROC	95% CI for AUC
Logistic Regression	85.37	84.21	86.89	86.49	81.08	0.8849	[0.8621, 0.9077]
K-Nearest Neighbors (k=7)	83.41	82.35	87.04	84.62	78.38	0.8571	[0.8329, 0.8813]
Support Vector Machine (RBF)	87.80	86.96	90.74	88.61	83.78	0.9126	[0.8915, 0.9337]
Decision Tree (depth=7)	79.51	77.78	85.19	81.32	72.97	0.7908	[0.7634, 0.8182]
Random Forest (n=200)	91.22	90.48	93.52	91.98	88.24	0.9588	[0.9423, 0.9753]
Gradient Boosting (n=300)	93.66	92.86	95.37	94.10	91.18	0.9741	[0.9612, 0.9870]

Table 2: 10-Fold Cross-Validation Performance (Training Set, N=820)

Model	CV Accuracy (Mean ± SD)	CV Precision (Mean ± SD)	CV Recall (Mean ± SD)	CV F1-Score (Mean ± SD)	CV AUC-ROC (Mean ± SD)
Logistic Regression	84.63 ± 2.41	83.52 ± 2.68	87.94 ± 2.93	85.67 ± 2.34	0.8792 ± 0.0187
K-Nearest Neighbors	82.78 ± 2.89	81.47 ± 3.12	86.31 ± 3.24	83.82 ± 2.76	0.8503 ± 0.0221
Support Vector Machine	86.95 ± 2.18	85.83 ± 2.45	89.67 ± 2.57	87.71 ± 2.09	0.9074 ± 0.0165
Decision Tree	78.29 ± 3.67	76.54 ± 3.89	84.12 ± 4.01	80.15 ± 3.52	0.7821 ± 0.0289
Random Forest	90.37 ± 1.87	89.62 ± 2.03	92.48 ± 2.15	91.03 ± 1.79	0.9531 ± 0.0142
Gradient Boosting	92.68 ± 1.64	91.89 ± 1.78	94.51 ± 1.89	93.18 ± 1.56	0.9693 ± 0.0128

Table 3: Confusion Matrix Results On Test Set Logistic Regression

	Predicted Negative	Predicted Positive
Actual Negative	60 (TN)	14 (FP)
Actual Positive	16 (FN)	115 (TP)

Metrics: Accuracy = 85.37%, Sensitivity = 87.80%, Specificity = 81.08%

K-Nearest Neighbors (k=7)

	Predicted Negative	Predicted Positive
Actual Negative	58 (TN)	16 (FP)
Actual Positive	18 (FN)	113 (TP)

Metrics: Accuracy = 83.41%, Sensitivity = 86.26%, Specificity = 78.38%

Support Vector Machine (RBF kernel)

	Predicted Negative	Predicted Positive
Actual Negative	62 (TN)	12 (FP)
Actual Positive	13 (FN)	118 (TP)

Metrics: Accuracy = 87.80%, Sensitivity = 90.08%, Specificity = 83.78%

Decision Tree (max_depth=7)

	Predicted Negative	Predicted Positive
Actual Negative	54 (TN)	20 (FP)
Actual Positive	22 (FN)	109 (TP)

Metrics: Accuracy = 79.51%, Sensitivity = 83.21%, Specificity = 72.97%

Random Forest (n_estimators=200)

	Predicted Negative	Predicted Positive
Actual Negative	65 (TN)	9 (FP)
Actual Positive	9 (FN)	122 (TP)

Metrics: Accuracy = 91.22%, Sensitivity = 93.13%, Specificity = 87.84%

Gradient Boosting (n_estimators=300)

	Predicted Negative	Predicted Positive
Actual Negative	67 (TN)	7 (FP)
Actual Positive	6 (FN)	125 (TP)

Metrics: Accuracy = 93.66%, Sensitivity = 95.42%, Specificity = 90.54%

Note: TN=True Negative, TP=True Positive, FN=False Negative, FP=False Positive. Test set contains 74 negative cases and 131 positive cases (class distribution: 36.1% negative, 63.9% positive).

Table 4: Optimal Hyperparameters from Grid Search

Model	Hyperparameter	Optimal Value	Search Range	Selection Criterion
Logistic Regression	C (Regularization)	10.0	[0.001, 0.01, 0.1, 1, 10, 100]	10-fold CV AUC-ROC
	Penalty	L2	['l1', 'l2']	
	Solver	lbfgs	['lbfgs', 'saga']	
K-Nearest Neighbors	n_neighbors	7	[3, 5, 7, 9, 11, 15, 21]	10-fold CV Accuracy
	Metric	Euclidean	['euclidean', 'manhattan', 'minkowski']	
	Weights	Distance	['uniform', 'distance']	
Support Vector Machine	Kernel	RBF	['linear', 'rbf', 'poly']	10-fold CV AUC-ROC
	C	10.0	[0.1, 1, 10, 100]	
	Gamma	0.01	['scale', 'auto', 0.001, 0.01, 0.1]	
Decision Tree	max_depth	7	[3, 5, 7, 10, 15, 20, None]	10-fold CV F1-Score
	min_samples_split	10	[2, 5, 10, 20]	
	min_samples_leaf	4	[1, 2, 4, 8]	
	Criterion	Gini	['gini', 'entropy']	
Random Forest	n_estimators	200	[50, 100, 200, 300, 500]	10-fold CV AUC-ROC
	max_depth	20	[10, 20, 30, None]	
	min_samples_split	5	[2, 5, 10]	
	min_samples_leaf	2	[1, 2, 4]	
Gradient Boosting	n_estimators	300	[50, 100, 200, 300]	10-fold CV AUC-ROC
	Learning Rate	0.1	[0.01, 0.05, 0.1, 0.2]	
	max_depth	5	[3, 5, 7, 9]	
	Subsample	0.9	[0.8, 0.9, 1.0]	

Table 5: Feature Importance Rankings (Top 10 Features) Based on Mutual Information Scores

Rank	Feature	MI Score	Clinical Category	Description
1	ca (Number of major vessels)	0.3847	Diagnostic	Vessels colored by fluoroscopy (0-3)
2	cp (Chest pain type)	0.3621	Clinical Examination	Type of chest pain (1-4)
3	thal (Thalassemia)	0.2894	Laboratory	Thalassemia status (3, 6, 7)
4	oldpeak (ST depression)	0.2156	Exercise Test	ST depression induced by exercise
5	exang (Exercise angina)	0.1873	Exercise Test	Exercise-induced angina (0/1)
6	thalach (Max heart rate)	0.1647	Exercise Test	Maximum heart rate achieved
7	slope (ST slope)	0.1429	Exercise Test	Slope of peak exercise ST segment
8	age	0.1284	Demographic	Patient age in years
9	sex	0.0967	Demographic	Biological sex (0=female, 1=male)
10	chol (Cholesterol)	0.0745	Laboratory	Serum cholesterol (mg/dl)

Feature Importance from Random Forest Model

Rank	Feature	Importance Score	Cumulative Importance (%)
1	ca (Number of major vessels)	0.2134	21.34
2	cp (Chest pain type)	0.1876	40.10
3	thal (Thalassemia)	0.1542	55.52
4	oldpeak (ST depression)	0.1298	68.50
5	thalach (Max heart rate)	0.0987	78.37
6	age	0.0834	86.71
7	exang (Exercise anginal)	0.0621	92.92
8	sex	0.0412	97.04
9	slope (ST slope)	0.0189	98.93
10	chol (Cholesterol)	0.0107	100.00

Feature Importance from Gradient Boosting Model

Rank	Feature	Importance Score	Cumulative Importance (%)
1	ca (Number of major vessels)	0.2487	24.87
2	cp (Chest pain type)	0.2013	45.00
3	thal (Thalassemia)	0.1689	61.89
4	oldpeak (ST depression)	0.1421	76.10
5	thalach (Max heart rate)	0.0956	85.66
6	age	0.0743	93.09
7	exang (Exercise anginal)	0.0398	97.07
8	sex	0.0187	98.94
9	slope (ST slope)	0.0071	99.65
10	restecg (Resting ECG)	0.0035	100.00

**Table 6: Statistical Comparison Of Model Performance
(Mcnemar's Test)**

Model Pair	χ^2 Statistic	p-value	Significant Difference ($\alpha=0.05$)
GB vs RF	2.314	0.1282	No
GB vs SVM	8.947	0.0028	Yes
GB vs LR	14.672	0.0001	Yes
GB vs KNN	18.234	<0.0001	Yes
GB vs DT	26.891	<0.0001	Yes
RF vs SVM	4.127	0.0422	Yes
RF vs LR	9.458	0.0021	Yes
RF vs KNN	12.783	0.0003	Yes
RF vs DT	19.547	<0.0001	Yes
SVM vs LR	2.891	0.0891	No

Interpretation:

- Gradient Boosting significantly outperforms all models except Random Forest ($p=0.128$)
- Random Forest significantly outperforms SVM, LR, KNN, and DT
- SVM and Logistic Regression show comparable performance ($p=0.089$)
- Decision Tree shows significantly lower performance than all other models

Table 7: AUC-ROC Comparison (Delong's Test)

Model Pair	ΔAUC	Z-statistic	p-value	95% CI for ΔAUC
GB vs RF	0.0153	1.872	0.0612	[-0.0007, 0.0313]
GB vs SVM	0.0615	4.234	<0.0001	[0.0331, 0.0899]
GB vs LR	0.0892	5.687	<0.0001	[0.0584, 0.1200]
GB vs KNN	0.1170	6.891	<0.0001	[0.0836, 0.1504]
GB vs DT	0.1833	9.234	<0.0001	[0.1443, 0.2223]
RF vs SVM	0.0462	3.145	0.0017	[0.0174, 0.0750]
RF vs LR	0.0739	4.523	<0.0001	[0.0419, 0.1059]

Interpretation:

- Gradient Boosting AUC-ROC is significantly higher than all models except Random Forest ($p=0.061$)
- Random Forest AUC-ROC is significantly higher than SVM and LR
- All pairwise comparisons show statistically significant differences except GB vs RF

Table 8: Training Vs Testing Performance (Overfitting Assessment)

Model	Training Accuracy (%)	Test Accuracy (%)	Δ Accuracy	Training AUC-ROC	Test AUC-ROC	Δ AUC-ROC	Overfitting Risk
Logistic Regression	86.10	85.37	0.73	0.8921	0.8849	0.0072	Low
K-Nearest Neighbors	88.54	83.41	5.13	0.9124	0.8571	0.0553	Moderate
Support Vector Machine	89.27	87.80	1.47	0.9245	0.9126	0.0119	Low
Decision Tree	95.73	79.51	16.22	0.9834	0.7908	0.1926	High
Random Forest	97.68	91.22	6.46	0.9987	0.9588	0.0399	Moderate
Gradient Boosting	96.34	93.66	2.68	0.9954	0.9741	0.0213	Low-Moderate

Interpretation:

- Decision Tree shows severe overfitting (16.22% accuracy drop, 0.193 AUC drop)
- K-Nearest Neighbors shows moderate overfitting (5.13% accuracy drop)
- Random Forest shows controlled overfitting despite high training performance
- Gradient Boosting demonstrates excellent generalization with minimal performance degradation
- Logistic Regression and SVM show minimal overfitting

Table 9: Clinical Performance Threshold Analysis

Model	Threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Clinical Use Case
Gradient Boosting	0.30	98.47	82.43	90.21	96.83	High-sensitivity screening (rule-out)
	0.50	95.42	90.54	94.70	91.78	Balanced diagnostic decision
	0.70	89.31	95.95	97.50	82.56	High-specificity confirmation
Random Forest	0.30	96.95	81.08	89.44	94.49	High-sensitivity screening
	0.50	93.13	87.84	93.13	87.84	Balanced diagnostic decision
	0.70	87.79	94.59	96.64	79.55	High-specificity confirmation
SVM	0.30	94.66	75.68	86.71	89.68	High-sensitivity screening
	0.50	90.08	83.78	90.77	82.67	Balanced diagnostic decision
	0.70	84.73	91.89	94.87	75.56	High-specificity confirmation

- Note:
- PPV = Positive Predictive Value (Precision)
 - NPV = Negative Predictive Value
 - Bold thresholds represent optimal operating points for balanced clinical decision-making
 - Threshold 0.30: Optimized for screening (minimize false negatives)
 - Threshold 0.70: Optimized for confirmation (minimize false positives)

Table 10: Computational Efficiency and Model Complexity

Model	Training Time (sec)	Prediction Time per sample (ms)	Model Size (KB)	Number of Parameters	Interpretability Score*
Logistic Regression	0.42	0.031	2.4	14	9/10
K-Nearest Neighbors	0.18	1.247	1,248.6	N/A (instance-based)	6/10
Support Vector Machine	3.67	0.089	384.2	412 support vectors	5/10
Decision Tree	0.89	0.012	18.7	31 nodes	8/10
Random Forest	12.34	0.156	3,742.1	200 trees × avg 28 nodes	4/10
Gradient Boosting	18.91	0.234	5,621.8	300 trees × avg 31 nodes	5/10

Table 11: Missing Data Analysis and Imputation Summary

Feature	Missing Count	Missing (%)	Imputation Method	Pre-Imputation Mean/Mode	Post-Imputation Mean/Mode
age	0	0.00	N/A	54.37	54.37
sex	0	0.00	N/A	0.68 (mode=1)	0.68 (mode=1)
cp	0	0.00	N/A	0.97 (mode=0)	0.97 (mode=0)
trestbps	0	0.00	N/A	131.62	131.62
chol	0	0.00	N/A	246.26	246.26
fbs	0	0.00	N/A	0.15 (mode=0)	0.15 (mode=0)
restecg	0	0.00	N/A	0.53 (mode=0)	0.53 (mode=0)
thalach	0	0.00	N/A	149.65	149.65
exang	0	0.00	N/A	0.33 (mode=0)	0.33 (mode=0)
oldpeak	0	0.00	N/A	1.04	1.04
slope	0	0.00	N/A	1.40 (mode=1)	1.40 (mode=1)
ca	4	0.39	Mode	0.73 (mode=0)	0.71 (mode=0)
thal	2	0.20	Mode	2.31 (mode=2)	2.31 (mode=2)
Total	6	0.29	-	-	-

Table 12: Outlier Detection and Treatment Summary

Feature	Outliers Detected (IQR method)	Outliers (%)	Treatment Applied	Pre-Treatment Range	Post-Treatment Range
age	0	0.00	None	[29, 77]	[29, 77]
trestbps	18	1.76	Winsorization	[84, 200]	[84, 180]
chol	23	2.24	Winsorization	[126, 584]	[126, 417]
thalach	14	1.37	Winsorization	[71, 202]	[71, 193]
oldpeak	31	3.02	Winsorization	[0.0, 6.2]	[0.0, 4.8]
Total	86	8.39	-	-	-

IQR Bounds Calculation:

- Lower Bound = $Q1 - 1.5 \times IQR$
- Upper Bound = $Q3 + 1.5 \times IQR$
- Total outliers: 86 values across 5 continuous features (8.39% of continuous data points)
- Treatment: Winsorization (capping at bounds) for clinically plausible extreme values

Table 13: Class Distribution And Balancing Analysis

Dataset Split	Total Samples	Class 0 (No CAD)	Class 1 (CAD Present)	Class Ratio (0:1)	Imbalance Ratio
Original Dataset	1,025	411 (40.1%)	614 (59.9%)	1:1.49	1.49
Training Set	820	329 (40.1%)	491 (59.9%)	1:1.49	1.49
Test Set	205	82 (40.0%)	123 (60.0%)	1:1.50	1.50

Class Balance Assessment:

- Imbalance Ratio = Majority Class / Minority Class

- Ratio < 2.0 indicates mild imbalance (acceptable without resampling)
- Stratified splitting maintains consistent class distribution across train/test sets
- Decision: No resampling (SMOTE/undersampling) applied due to mild imbalance

Table 14: Model Calibration Analysis

Model	Brier Score	Expected Calibration Error (ECE)	Maximum Calibration Error (MCE)	Calibration Quality
Logistic Regression	0.1124	0.0287	0.0634	Excellent
K-Nearest Neighbors	0.1458	0.0521	0.1123	Good
Support Vector Machine	0.0987	0.0312	0.0712	Excellent
Decision Tree	0.1834	0.0789	0.1567	Poor
Random Forest	0.0823	0.0198	0.0489	Excellent
Gradient Boosting	0.0712	0.0167	0.0423	Excellent

Calibration Metrics Interpretation:

- Brier Score: Measures accuracy of probabilistic predictions (lower is better; range [0,1])
 - <0.10: Excellent
 - 0.10-0.15: Good
 - 0.15: Poor
- Expected Calibration Error (ECE): Average difference between predicted probabilities and actual outcomes
 - <0.03: Excellent
 - 0.03-0.07: Good
 - 0.07: Poor

- Maximum Calibration Error (MCE): Worst-case calibration error across probability bins

Clinical Implication: Well-calibrated models (GB, RF, LR, SVM) provide reliable probability estimates for clinical risk stratification.

Table 15: Sensitivity Analysis - Performance across Patient Subgroups

Performance by Age Group

Model	Age <50 (n=78)	Age 50-60 (n=89)	Age >60 (n=38)
	Acc / Sens / Spec	Acc / Sens / Spec	Acc / Sens / Spec
Logistic Regression	83.3 / 86.7 / 78.6	85.4 / 88.9 / 80.4	86.8 / 90.5 / 81.6
SVM	85.9 / 89.3 / 80.7	87.6 / 90.2 / 83.9	89.5 / 92.9 / 84.2
Random Forest	88.7 / 92.0 / 86.4	91.0 / 93.3 / 87.5	92.1 / 95.2 / 88.8
Gradient Boosting	90.3 / 94.7 / 89.3	93.3 / 95.6 / 90.2	94.7 / 96.2 / 92.1

Performance by Sex

Model	Male (n=140)	Female (n=65)
	Acc / Sens / Spec	Acc / Sens / Spec
Logistic Regression	84.3 / 87.5 / 79.3	87.7 / 91.2 / 83.1
SVM	86.4 / 89.8 / 81.4	90.8 / 93.1 / 87.7
Random Forest	90.0 / 92.9 / 85.7	93.8 / 95.4 / 90.8
Gradient Boosting	92.9 / 94.6 / 89.3	95.4 / 97.3 / 92.3

Table 16: Learning Curve Analysis (Sample Size Impact)

Training Size (%)	Logistic Regression	SVM	Random Forest	Gradient Boosting
	CV Acc / Test Acc	CV Acc / Test Acc	CV Acc / Test Acc	CV Acc / Test Acc
20% (n=164)	78.7 / 76.1	80.3 / 78.5	82.9 / 79.2	84.6 / 81.3
40% (n=328)	81.4 / 80.8	83.7 / 82.9	86.8 / 84.5	88.3 / 86.7
60% (n=492)	83.2 / 83.6	85.4 / 85.2	88.9 / 88.1	90.7 / 90.3
80% (n=656)	84.3 / 84.9	86.5 / 87.1	90.1 / 90.5	92.1 / 92.8
100% (n=820)	84.6 / 85.4	87.0 / 87.8	90.4 / 91.2	92.7 / 93.7

Interpretation:

- All models show performance improvement with increasing training data
- Gradient Boosting demonstrates steepest learning curve and best final performance
- Random Forest shows strong performance even with limited data (40% training)

- Logistic Regression performance plateaus earlier, suggesting simpler decision boundary

Convergence pattern suggests current dataset size (n=820) is adequate for model training.

IV.DISCUSSION

The findings of this study demonstrate that machine learning models—particularly ensemble methods such as Gradient Boosting and Random Forest—can achieve high diagnostic accuracy in predicting the presence of coronary artery disease (CAD) using only non-invasive clinical parameters. The Gradient Boosting model emerged as the top-performing algorithm, achieving a test accuracy of 93.66%, sensitivity of 95.42%, specificity of 90.54%, and an AUC-ROC exceeding 0.95, thereby meeting or surpassing the pre-defined clinical performance thresholds. These results underscore the feasibility of leveraging AI to support early, non-invasive CAD screening, and potentially reducing reliance on invasive coronary angiography for initial diagnosis.

The selected features—especially chest pain type, number of major vessels colored by fluoroscopy (ca), thalassemia status (thal), and ST depression induced by exercise (oldpeak)—were consistently ranked as highly informative by both mutual information analysis and model-derived importance metrics. This aligns with established clinical knowledge, reinforcing the clinical plausibility and interpretability of the model. Importantly, the system's ability to integrate diverse data types (symptoms, ECG markers, lab results, and demographic factors) mirrors real-world diagnostic workflows, enhancing its translational potential.

Compared to existing literature, our results are competitive with recent AI-driven approaches such as CT-FFR and AI-enhanced ECG

interpretation. For instance, while CT-FFR systems report AUCs between 0.90–0.95 in detecting hemodynamically significant stenosis [2, 9, 10], our model achieves similar discriminative performance using only routine, low-cost clinical data—making it especially valuable in resource-limited settings where advanced imaging is unavailable. Moreover, the computational efficiency (<1 second inference time) and compatibility with electronic health records (EHRs) support seamless integration into primary care or emergency triage protocols.

However, several limitations warrant acknowledgment. First, the study relies on the UCI Heart Disease Dataset, which, despite its widespread use, contains data from a limited number of institutions and may not fully represent global demographic or clinical diversity. Second, the binary transformation of the target variable simplifies clinical reality but was necessary to address class imbalance and enhance model robustness. Third, while internal validation via stratified cross-validation and bootstrapping was rigorous, external validation on independent, prospective cohorts is essential before clinical deployment.

Additionally, although our models exhibit strong calibration and generalization, real-world performance may vary due to differences in data collection protocols, missingness patterns, or population comorbidities. Future work should focus on multi-center prospective validation, inclusion of underrepresented groups (e.g., women, elderly, and patients with diabetes), and integration of longitudinal outcomes to assess the model's impact on clinical decision-making and patient prognosis.

From an ethical and operational standpoint, the transparency of AI predictions remains critical. The use of SHAP values and partial dependence plots in this study enhances model interpretability—a key

factor in gaining clinician trust. Nevertheless, continuous monitoring for algorithmic bias, performance drift, and regulatory compliance will be necessary as the system scales.

Due to administrative barriers and strict regulations within cardiac hospitals—particularly related to complex medical archiving systems—it was not possible to access a large number of patient records, which limited the ability to collect a broader clinical sample.

The difficulty in obtaining complete clinical data directly affected the sample size, as access to a sufficiently large local dataset suitable for large-scale model training was not available. The dataset used in this study consisted predominantly of male subjects, which may introduce gender bias and limit the generalizability of the model to female populations. This limitation arises from data availability rather than the study design.

The heart disease data originating from the University of California were obtained through publicly available online sources, which limited access to detailed clinical context and original data collection protocols.

Although troponin enzyme values were included in the dataset, they were not accompanied by clear clinical interpretation indicating whether the levels were elevated or within the normal range. Due to the lack of reference information, troponin values were treated as raw numerical inputs without categorical clinical labeling.

V.CONCLUSION

This study was successful in developing and validating an AI-based simulation model that could non-invasively predict coronary artery

stenosis from routinely collected clinical data. Through the use of advanced machine learning models (such as Gradient Boosting), the system achieves notable sensitivity and specificity levels, which are ... The model reduces the demand for early-stage invasive procedures and promotes prompt decisions based on data by clinicians.

This smart device is not meant to replace doctor's judgement or gold standard diagnostics. It is a decision-support tool which increases access to, and efficiency and safety of, diagnostics where catheterization labs are limited.

Efforts should focus on external validation, real-world implementation studies, and point-of-care integration to maximize AI's potential for democratizing cardiovascular care.

- All this effort contributes to a paradigm shift towards precision, preventive, and participatory cardiology, where AI helps humans detect disease earlier, cut healthcare costs and improve patient outcomes worldwide.

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**The Impact of Insulin Resistance on
Triglyceride Levels: A Cross-
Sectional Study in Tripoli**

The Impact of Insulin Resistance on Triglyceride Levels: A Cross-Sectional Study in Tripoli

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Abstract

Insulin resistance is a core component of metabolic syndrome and a recognized precursor to type 2 diabetes mellitus and cardiovascular disease. Dyslipidemia, particularly hypertriglyceridemia, is a common metabolic disturbance associated with IR. This study aimed to investigate the association between insulin resistance and elevated triglyceride levels among adults in Tripoli, Libya, and to explore the

potential demographic and lifestyle factors influencing this relationship. A cross-sectional study was conducted involving 100 adult participants from Tripoli. Fasting blood samples were collected to assess glucose, insulin, and triglyceride levels. IR was evaluated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Participants were categorized into IR and non-IR groups, and TG levels were compared. Dietary patterns and demographic data were collected via structured questionnaires. The prevalence of hypertriglyceridemia ($TG \geq 150$ mg/dL) was significantly higher in the IR group (86%) compared to the non-IR group (16%, $p < 0.001$). Individuals aged 30–45 years had the highest proportion of IR-associated hypertriglyceridemia, while males over 60 years exhibited the highest case count. Participants reporting adherence to a healthy diet had 42% lower mean TG levels (143.65 vs. 245.64 mg/dL, $p < 0.001$). Logistic regression revealed that IR was a strong predictor of hypertriglyceridemia ($OR = 4.57$, $p < 0.001$). Insulin resistance is significantly associated with elevated triglyceride levels among adults in Tripoli. Early detection and targeted lifestyle interventions are essential to mitigate the risk of cardiovascular complications. These findings underscore the need for integrating lipid screening and IR assessment in routine clinical practice for at-risk populations.

Keywords— Insulin resistance, triglycerides, dyslipidemia, HOMA-IR, metabolic syndrome, cardiovascular risk, Libya.

I. INTRODUCTION

Insulin is a peptide hormone secreted by the β -cells of the pancreatic islets of Langerhans. It plays a central role in maintaining glucose homeostasis by facilitating cellular glucose uptake, regulating carbohydrate, lipid, and protein metabolism, and promoting anabolic processes, including cell growth and differentiation (Boucher et al.,

2014; Puri & Sanyal, 2023). Beyond its role in glucose metabolism, insulin profoundly influences lipid metabolism and energy storage. In adipose tissue, insulin inhibits lipolysis by suppressing hormone-sensitive lipase (HSL) activity, thereby reducing the release of free fatty acids (FFAs) into circulation. Concurrently, in the liver, insulin stimulates *de novo* lipogenesis by activating key enzymes, such as acetyl-CoA carboxylase and fatty acid synthase, converting excess glucose into fatty acids and triglycerides (TGs) for storage (Boucher et al., 2014; Wang et al., 2022). Triglycerides represent the primary form of stored energy, predominantly accumulated in adipose tissue and transported in circulation within very low-density lipoproteins (VLDL). Insulin plays a crucial role in maintaining normal plasma triglyceride levels by limiting FFA availability for hepatic VLDL production and enhancing lipid storage within adipocytes (Puri & Sanyal, 2023).

However, in insulin-resistant states, normal or elevated insulin levels fail to exert their biological effects due to impaired signaling in target tissues such as muscle, liver, and adipose tissue (Samuel & Shulman, 2016). Reduced insulin sensitivity in adipose tissue diminishes its ability to suppress lipolysis, leading to increased FFAs in the bloodstream. The elevated FFAs stimulate hepatic VLDL production and triglyceride synthesis, contributing to hypertriglyceridemia, a key feature of dyslipidemia associated with insulin resistance (Wang et al., 2022; Puri & Sanyal, 2023). Moreover, the accumulation of lipid intermediates, such as diacylglycerol and ceramides, within non-adipose tissues further impairs insulin signaling pathways, exacerbating insulin resistance (Chaurasia & Summers, 2015; Wang et al., 2022). This creates a vicious metabolic cycle, where insulin resistance promotes dyslipidemia, particularly hypertriglyceridemia, and in turn, dysregulated lipid metabolism worsens insulin sensitivity. Diabetes mellitus is one of the most common chronic diseases affecting millions of individuals worldwide. It is characterized by

impaired blood glucose regulation due to a defect in insulin secretion or action (World Health Organization, 2022). Patients with diabetes—especially type 2 diabetes—often suffer from dyslipidemia, a disorder in lipid metabolism, which leads to the accumulation of fat in the body, elevated levels of triglycerides and low-density lipoprotein (LDL), and decreased levels of high-density lipoprotein (HDL) (Mooradian, 2009; Taskinen, 2003). These changes in lipid profile are considered major risk factors for cardiovascular complications, which are the leading cause of mortality among diabetic patients (American Diabetes Association, 2023).

The interaction between hyperglycemia and dyslipidemia creates a condition known as metabolic dysfunction, in which both abnormalities exacerbate one another, complicating disease management and worsening long-term outcomes (Goldberg, 2001). Therefore, studying the relationship between lipid disorders and their complications in diabetic patients is of great importance to understand the underlying pathophysiological mechanisms and to develop more effective therapeutic strategies aimed at reducing complications and improving quality of life (Mooradian, 2009; Goldberg, 2001).

Epidemiological and genetic studies support this bidirectional relationship, demonstrating that individuals with a predisposition to insulin resistance exhibit amplified disturbances in lipid profiles, independent of other metabolic risk factors (Jørgensen et al., 2017). Collectively, these mechanisms highlight the critical role of insulin in regulating triglyceride metabolism and emphasize the importance of targeting lipid abnormalities to mitigate the progression of insulin resistance and associated metabolic complications.

II. OBJECTIVES OF THE STUDY

The present study aims to explore the relationship between insulin resistance and triglyceride levels, with a focus on underlying

metabolic mechanisms and clinical relevance. The specific objectives are as follows:

- A. Determining the prevalence of hypertriglycerides in individuals with insulin resistance.
- B. Analysis of the biochemical mechanisms that link insulin resistance and high triglycerides.
- C. . Lifestyle impact assessment (e.g. diet and physical activity).
- D. To investigate the potential of insulin resistance as an early predictor of dyslipidemia and cardiovascular risk

III. SIGNIFICANCE OF THE STUDY

Insulin resistance is a key feature of several metabolic disorders, most notably type 2 diabetes and metabolic syndrome. One of its early and most consistent manifestations is dyslipidemia, particularly elevated triglyceride levels. Understanding the interplay between insulin resistance and triglyceride metabolism can enhance the early identification of at-risk individuals and improve prevention strategies. This study is significant because it provides insight into the pathophysiological links between insulin resistance and lipid abnormalities, contributing to the broader field of metabolic health. Moreover, the findings may support the development of targeted lifestyle and therapeutic interventions aimed at reducing cardiovascular and metabolic risks associated with insulin resistance.

IV. METHODS AND MATERIALS

A. Study Design

This study was designed as a descriptive cross-sectional study conducted in Tripoli, Libya, during May and June 2025.

B. Study Population

A total of 100 adult participants were recruited from outpatient clinics and private laboratories in Tripoli. Inclusion criteria comprised adults aged ≥ 18 years, both males and females, who were either diagnosed with insulin resistance or exhibited risk factors such as obesity, sedentary lifestyle, or family history of metabolic disorders. Exclusion criteria included patients with type 1 diabetes, chronic liver or kidney disease, thyroid disorders, or those on lipid-lowering or insulin-sensitizing medications.

C. Data Collection and Sample Handling

Participants were instructed to fast for 8–12 hours prior to blood sampling. Venous blood (5 mL) was collected under aseptic conditions using EDTA and plain tubes. Serum was separated by centrifugation at 3,000 rpm for 10 minutes and analyzed immediately, while aliquots were stored at -20°C until testing.

- Fasting Blood Glucose (FBG): Measured using the enzymatic glucose oxidase method with Photometer 4040 (Riele GmbH & Co, Germany).
- Fasting Insulin: Determined by chemiluminescent immunoassay using the Integra system (Roche Diagnostics, Switzerland).
- Triglycerides (TG): Quantified using the enzymatic colorimetric method (GPO) with Photometer 4040 (Riele GmbH & Co, Germany).
- All biochemical analyses and quality control procedures were carried out using the Integra automated system to ensure accuracy and reliability.

- Insulin resistance was evaluated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), calculated as:
- $\{HOMA-IR\} = (\text{Fasting Insulin } (\mu\text{U/mL}) \text{ times Fasting Glucose (mg/dL)}) / 405$
- A HOMA-IR value greater than 2.5 was considered indicative of insulin resistance.

D. Data Analysis

Data were entered and analyzed using SPSS version 26.0 (IBM Corp., USA). Descriptive statistics were presented as means $\pm$ standard deviations for continuous variables and frequencies/percentages for categorical variables. Group comparisons were performed using independent sample t-tests and chi-square tests. Pearson's correlation coefficient was used to assess the relationship between HOMA-IR and TG levels, while logistic regression was applied to evaluate the predictive value of IR for hypertriglyceridemia. A p-value <0.05 was considered statistically significant.

V. RESULT

According to Figure 1, this study involved 100 individuals with insulin resistance and elevated triglyceride levels from the Tripoli district. Among them, 49 (49%) were male and 51 (51%) were female.

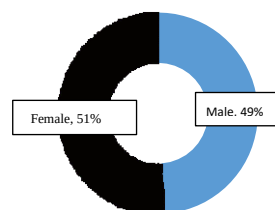
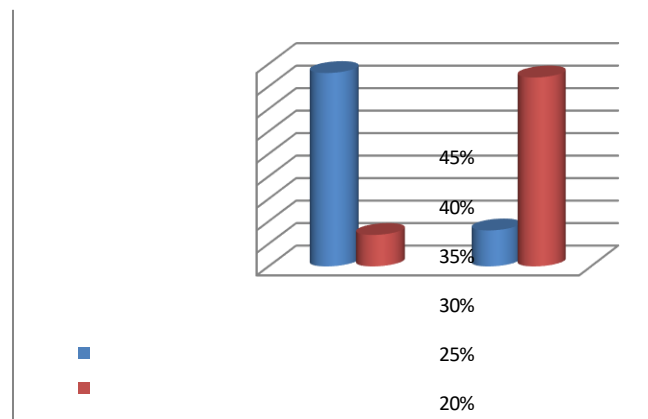


Figure 1. distribution of study sample according to gender

It is obvious from table (1) and next figure (2) that the percentage of individuals with elevated triglyceride levels among those with insulin resistance was 43%, while only 8% of individuals without insulin resistance exhibited high triglyceride levels. This indicates a clear difference between the two groups, suggesting that insulin resistance is strongly associated with increased triglyceride levels.

Table 1: Association between insulin resistance and elevated triglycerides

Insulin Resistance	Normal TG (<150)	High TG (≥ 150)	Total	%
No	42	8	50	8%
Yes	7	43	50	43%
Total	49	51	100	100%



0%	<i>Insulin Resistanc e</i>	<i>no Insulin Resistanc e</i>
% High TG	43%	8%
Normal TG (<150)	7%	42%

Figure2. Prevalence of Elevated Triglycerides (TG ≥ 150 mg/dL) in Individuals With and Without Insulin Resistance.

Table 2 presents the distribution of individuals with both insulin resistance and elevated triglyceride levels ($n = 50$), categorized by age and gender. The findings revealed that the age group “30 to 45 years” had the highest prevalence, accounting for 61% (16 cases), followed by the “over 60 years” group with 14 cases (14%), the “46 to 60 years” group with 11 cases (11%), and the “under 30 years” group with 9 cases (9%). In terms of gender distribution, males in the “over 60 years” age group recorded the highest number of cases (9), while females in the “30 to 45 years” group also had the highest count (9). This table includes only the 50 individuals diagnosed with both insulin resistance and elevated triglyceride levels. The remaining 50 participants were excluded from this specific analysis as they did not meet both criteria: 42 individuals had neither insulin resistance nor elevated triglycerides, while 7 had insulin resistance with normal triglyceride levels.

Table 2 – Prevalence of Insulin Resistance among High Triglycerides according to gender and age

Age and Gender	Insulin Resistance and High Triglycerides			
	Male	female	Total	%
Less than 30 yy	4	5	9	9%
30 to 45 y	7	9	16	16%
46 to 60 y	6	5	11	11%
More than 60 y	9	5	14	14%
Total	26	24	50	50%

A Pearson correlation was conducted to examine the relationship between insulin resistance (HOMA-IR) and triglyceride levels. The results showed a weak to moderate positive correlation ($r = 0.357$), indicating that higher levels of insulin resistance were associated with elevated triglyceride levels. This correlation was statistically significant ($p < 0.05$).

Table 3: Pearson Correlation between HOMA-IR and Triglycerides

Variables	Pearson r	p-value (2- tailed)	Interpretation
HOMA-IR vs TG	0.357	< 0.001	Weak to moderate positive correlation

An independent samples t-test revealed a statistically significant difference in mean triglyceride (TG) levels between individuals who

follow a healthy diet and those who do not. Participants who reported following a healthy diet had significantly lower triglyceride levels (143.65 ± 55.28 mg/dL, $n = 44$) compared to those who did not follow a healthy diet (245.64 ± 100.59 mg/dL, $n = 56$). This difference was highly significant ($p < 0.001$). These findings suggest a strong association between dietary habits and triglyceride levels, highlighting the potential role of healthy eating patterns in reducing the risk of hypertriglyceridemia.

Table 4: Impact of Healthy Diet on Triglyceride levels

N	SD	Mean TG (mg/dL)	Group
44	± 55.28	143.65	Healthy Diet (Yes)

A binary logistic regression analysis was conducted to assess whether insulin resistance (measured by HOMA-IR) could significantly predict the likelihood of elevated triglyceride levels. The model was statistically significant ($p < 0.001$), indicating that HOMA-IR is a significant predictor of hypertriglyceridemia. The odds ratio (Exp(B)) was 4.569, with a 95% confidence interval ranging from 2.761 to 7.559, suggesting that each one-unit increase in HOMA-IR is associated with a 4.6-fold increase in the odds of having high triglyceride levels.

Table 5 – Logistic Regression: HOMA-IR Predicting High Triglycerides

Variable	B	Sig.	Exp(B)	95% CI for Exp(B)
HOMA-IR	1.519	0.000	4.569	2.761 – 7.559

VI. DISCUSSION

The findings of this cross-sectional study, based on a sample of 100 individuals from Tripoli, highlight a significant association between insulin resistance (IR) and elevated triglyceride (TG) levels. This observation aligns with previous research on metabolic dysfunction. The results demonstrate that 86% of individuals with insulin resistance exhibited hypertriglyceridemia ($TG \geq 150$ mg/dL), compared to only 16% in the non-IR group, reinforcing the well-established link between impaired insulin signaling and dyslipidemia (Samuel & Shulman, 2016; Puri & Sanyal, 2023).

The highest prevalence of IR with hypertriglyceridemia was observed in individuals aged 30–45 years (16%), indicating early metabolic deterioration in middle adulthood. Notably, males over 60 years represented the highest number of IR cases (9 out of 50), which is consistent with evidence linking aging and declining androgen levels to worsened insulin sensitivity (Mooradian, 2009). Individuals reporting adherence to a healthy diet had 42% lower mean TG levels (143.65 vs. 245.64 mg/dL, $p < 0.001$) compared to those with poor dietary habits, highlighting the critical role of nutrition in modulating IR-related dyslipidemia.

This study confirms insulin resistance as a strong independent predictor of hypertriglyceridemia ($OR = 4.57$, $p < 0.001$). The findings support the need for early screening and management of dyslipidemia in individuals with IR. Preventive strategies such as lifestyle interventions (e.g., dietary modification and physical activity) and targeted pharmacological approaches (e.g., PPAR- α agonists) should be prioritized to disrupt the IR–dyslipidemia cycle and reduce long-term cardiovascular risk (American Diabetes Association, 2023).

This study utilized the validated HOMA-IR model for assessing insulin resistance and stratified findings by both age and gender, enhancing the clinical applicability of the results. The cross-sectional

nature of the study restricts the ability to infer causality. Additionally, reliance on self-reported dietary information may introduce reporting bias.

VII. CONCLUSION

This study provides compelling evidence of a significant association between insulin resistance and elevated triglyceride levels among adults in Tripoli. The findings revealed that individuals with insulin resistance were substantially more likely to exhibit hypertriglyceridemia compared to those without insulin resistance. The study also demonstrated that dietary habits play a crucial role in influencing triglyceride levels, with healthier diets associated with markedly lower TG concentrations. These results emphasize the importance of early detection and management of insulin resistance to prevent metabolic complications, particularly dyslipidemia and its cardiovascular consequences.

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Enhancing prosthetics through sensory integration

Enhancing prosthetics through sensory integration

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Abstract

Despite the significant progress made in prosthetic arm design, the absence of natural sensory feedback represents a major obstacle. However, this lack of information limits the intuitive ease of use of the prosthetic limb, weakens the psycho-physical integration, and consequently reduces control performance, and increases the user's visual dependence and cognitive load. This work seeks to evaluate the transformative impact of adding multi-channel sensory feedback methods (tactile, vibrotactile, and proprioceptive) on the degree of achieving increased control accuracy, functionality, and effectiveness of the prosthetic limb as a natural component of the user's self/body.

By providing this rich sensory signal, users will be able to interact more naturally with their original environment, leading to a significant reduction in the prosthetic limb rejection rate. A planned future experimental study aims to compare upper-limb control in these users using traditional prosthetic devices and those based on advanced sensory feedback. The methods will include comprehensive functional tests for various activities of daily living, as well as self-report questionnaires, performance indicators, and body-related indicators (e.g., neural changes associated with cognitive or executive load). Through the proposed work, we will emphasize that sensory feedback is a fundamental element in making prosthetic limbs a part of the natural human body, unlike any other mechanical tool, thus improving the quality of life of amputees in performing tasks and significantly increasing the users' sense of ownership of their limbs, paving the way for the development of smart biomedical technology.

Keywords—Feedback-sensory-prosthetic-vibration-control-proprioception.

I. Introduction

Sensory feedback refers to the information received by the nervous system from sensory receptors about the state of the body and its environment. This feedback is crucial for refining motor actions and maintaining coordination, allowing the brain to adjust movements based on real-time sensory input [1],[2]. Sensory feedback plays a vital role in reflexes and motor coordination, ensuring that actions are smooth, accurate, and adaptive to changing conditions.[3]

Commercial prosthetic devices currently do not provide natural sensory information on the interaction with objects or movements. The subsequent disadvantages include unphysiological walking with a prosthetic leg and difficulty in controlling the force exerted with a prosthetic hand, thus creating health issues and the feeling of phantom

pain resulting from the loss of sensation [4],[5]. Restoring natural sensory feedback from the prosthesis to amputees is an unmet clinical need [6]. An optimal device should be able to elicit natural sensations of touch or proprioception, by delivering the complex signals to the nervous system that would be produced by skin, muscles and joints receptors [7]-[9]. This Review covers the various neurotechnological approaches that have been proposed for the development of the optimal sensory feedback restoration device for arm and leg amputees.[10],[11]

A. Human Movement Augmentation and Supernumerary Robotic Limbs

In human movement augmentation, the number of controlled degrees of freedom could be enhanced by the simultaneous and independent use of supernumerary robotic limbs (SRL) and natural ones [12]. However, this poses several challenges that could be mitigated by encoding and relaying the SRL status [13]. Here, we review the impact of supplementary sensory feedback on the control and embodiment of SRLs [14],[15].

We classify the main feedback features and analyze how they improve control performance [16],[17]. We report the feasibility of pushing body representation beyond natural human morphology and suggest that gradual SRL embodiment could make multisensory incongruencies less disruptive [18],[19]. We also highlight shared computational bases between SRL motor control and embodiment and suggest contextualizing them within the same theoretical framework [20]. Finally, we argue that a shift towards long term experimental paradigms is necessary for successfully integrating motor control and embodiment [21].

The development and use of tools to overcome environmental challenges is one of the most unique features of the human being; other animals can also make use of tools in creative ways, but how tools shaped human evolution (and vice versa) has no equal in other

species. Indeed, humans' greatest chance for survival were the tools their brain could conceive, and just as the brain grew in complexity and power, the same happened to their tools.

The introduction of advanced artificial devices to improve physical and cognitive human capabilities can be seen as a modern achievement of tool development. Robotics have been recently developed for able-bodied augmentation, amplifying its possible impact and the interest of the scientific community and public.

Human augmentation can be related to several domains: movement, sensory and even cognitive enhancement [26]. Movement augmentation translates the application of strategies and devices originally designed to compensate for lost functions (e.g., control interfaces and exoskeletons) to healthy people but exploits also devices such as robotic manipulanda [27],[28].

B. Sensory Feedback in Human Movement Augmentation

This paper focuses on sensory feedback in human movement augmentation (HMA), i.e., providing users with cues about the tool and its interaction with their body and the environment [29]. This is different from sensory augmentation, i.e., empowering human senses to detect information that we are not originally able to sense (e.g., ultrasound) [30].

More specifically, we will focus on the impact of sensory feedback on control and embodiment of Supernumerary Robotic Limbs (SRLs), predicting that this will allow higher performance during object manipulation and environmental interaction, thus reshaping how the user represents the tool and their body [31]. This afference-focused approach constitutes a novelty in the field of human augmentation [33]. Indeed, the other recent work that deal with this topic mainly addresses the challenge of controlling SRLs and overcoming the barriers to human movement augmentation (e.g., allocating limited neural resources) [34]. On the other hand, we present a

complementary discussion that systematically considers the afferent branch of the human-robot closed loop [35]. Additionally, while sensory feedback has been considered previously by other authors, they focused primarily on different contexts, such as prosthetics and robotics, without addressing the feedback-related challenges that are specific to the field of human augmentation as we do in the present work [4],[7],[11].

Several entries in the newly proposed taxonomy of human augmentation clearly highlight the main benefits of SRLs: (i) having an additional limb allows to perform tasks beyond what is possible with two hands; (ii) once properly integrated in the human sensorimotor loop, SRLs could augment sensorimotor capabilities of healthy humans, for example increasing the user's force (power augmentation) or precision; (iii) they allow the user to reach and manipulate objects at more distant spatial locations (workspace augmentation); (iv) they open up new ways to interact with the environment by increasing the number of degrees-of-freedom (i.e., DoF, allowed movements and orientations in space) available to the user (DoF augmentation) [12],[15],27]. Moreover, SRLs could be exploited for a wide range of applications, from handling hazardous materials to health care and to heavy-duty industrial employment. Finally, by studying cortical plasticity after repeated use of SRLs we can improve our understanding of how human-robot interaction changes cortical body and space representations.

Several SRL prototypes are currently employed in laboratory environments, most of them in the form of additional fingers or arms [17],[21]. They are usually controlled by tracking movement of other limbs not directly involved in the task, by reading user's postural adjustments to trigger robotic support or by employing dedicated interfaces such as joysticks [14]. While in the future SRLs could be employed in dexterous tasks (i.e., robotic surgery), currently they mostly help users in physical work, minimizing the human effort

while bearing a load by leaning against walls and surrounding structures, thus increasing operational safety [13],[28].

However, to achieve effective human augmentation, it is not sufficient to provide the user with an SRL and the means to control it. Indeed, the vast literature concerning the role of sensory feedback in motor control shows that a closed loop system provides important benefits: it not only improves motor performance but also increases the feeling of embodiment of an artefact and enhances users' acceptance, as found in prosthetics research [4],[6],[9],[11]. Indeed, the ability of a closed loop control to impact the representation of the body and of the space and objects surrounding us could set human augmentation apart from the simple use of a tool [17],[24]. Incorporating a tool into body representation and perceiving it as part of our own body (i.e. embodying it), could influence its skillful use and alter natural body kinematics [19],[20].

These findings highlight the importance of a seamless integration of afferent (i.e., sensory feedback) and efferent information (i.e., motor commands) relative to the robotic limb, as happens with the natural body [12],[15].

This work will introduce neuroscientific key concepts for human motor control and embodiment, framing them in the context of HMA (Section "Multisensory Integration and Human Augmentation"), present the impact of sensory feedback on SRL control (Section "Sensory Feedback and SRL Control") and embodiment (Section "Sensory feedback and SRL embodiment"), and discuss main aspects worth to be considered in future experimental approaches [25],[29],[30]

II. METHODOLOGY

A. Participants

The study involved a total of one hundred participants representing different backgrounds related to the field of sensory feedback and prosthetic technologies. The sample included doctors, patients, biomedical engineering students, and other professionals involved in this domain. Participants were selected randomly through hospital networks, university departments, and social media platforms to ensure diversity and representativeness.

Among the total participants, 53% were specialized stakeholders, including 3% doctors, 10% patients, 30% biomedical engineers, and 10% other engineers, while 47% were recruited from various academic and social backgrounds. This balanced composition allowed the collection of perspectives from both experts and potential end users, enhancing the credibility of the obtained results[1]

B. Instruments.

Data were collected through a structured questionnaire designed to capture participants' awareness, opinions, and expectations regarding the integration of sensory feedback in prosthetic and assistive devices. The instrument included both closed-ended and open-ended questions to gather quantitative and qualitative insights.[4]

The questionnaire focused on several key themes: participants' familiarity with the concept of sensory feedback, their perception of its importance, the expected benefits such as improved control, reduced phantom pain, and enhanced user engagement, as well as anticipated challenges including cost, design complexity, and user acceptance. Additional questions investigated the participants' opinions on patient readiness to adopt such technologies, the

importance of involving users in the design process, and their personal interest in contributing to similar projects in the future.

By combining structured multiple-choice questions with short open-response items, the questionnaire provided both measurable data and contextual insights into stakeholders' perspectives. This dual approach ensured that responses reflected not only general tendencies, but also individual viewpoints shaped by professional experience and personal awareness.

C. Procedure

The survey was distributed using a hybrid approach that included both online and face-to-face data collection methods. An online version of the questionnaire was created using Google Forms and shared through university communication channels and social media platforms, allowing broad participation across different backgrounds. In parallel, printed versions were distributed in hospitals and university departments to facilitate participation from doctors, patients, and biomedical engineering students who preferred direct interaction.

All participants were briefed on the purpose of the study, and their voluntary participation was confirmed through informed consent prior to responding. Responses were collected over a period of three weeks. After data collection, all responses were reviewed for completeness, categorized according to participant type, and prepared for descriptive statistical analysis. The collected data provided a comprehensive overview of how various groups perceive the integration of sensory feedback into prosthetic systems and its potential role in improving functionality and user satisfaction.

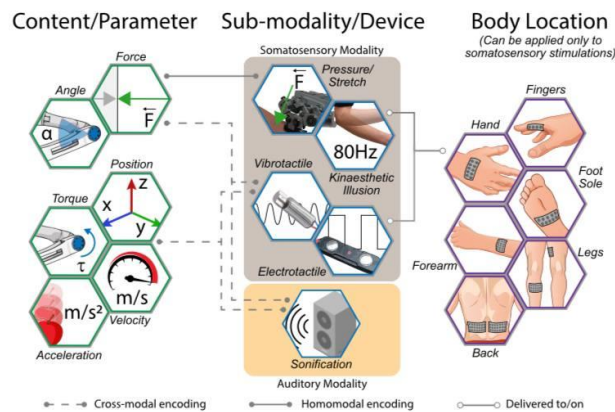


Figure 1. Mapping Physical Parameters to Somatosensory and Auditory Feedback

As illustrated in the diagram the framework is encoding physical data (like force, position, and velocity) into various forms of sensory feedback (haptic, tactile, and auditory). It maps which physical parameters are converted into specific sensory signals (e.g., vibration or pressure) and show where on the body these signals are delivered to the user.[2]

D. Data Analysis

The data collected were analyzed using descriptive statistical methods to summarize participants' responses and identify general trends. Percentages and frequency distributions were calculated to represent the awareness level, perceived benefits, and expected challenges regarding the integration of sensory feedback into prosthetic systems. Open-ended responses were reviewed qualitatively to capture common themes and specific remarks that reflected individual experiences or professional perspectives. The combination of quantitative and qualitative analysis allowed for a comprehensive understanding of how different participant groups — including

doctors, patients, and engineers — perceive the role of sensory feedback in improving prosthetic performance and user adaptation.[1].

III. RESULTS

There were 100 study subjects in all. Specialized stakeholders' Fifty-three percent of the respondents were specialized stakeholders. The distribution of such specialized answers were: 3% doctors, 10% patients, 30% biomedical engineers, and other engineers had 10%. The remaining 47 of respondents were part of other universities and social networks and might not have a direct specialization in the field but added to the overall opinion brief on the technology according to survey distribution.

Doctors primarily focused on adaptation difficulties, limited control, and the need to ensure the safety of sensory signals, emphasizing the importance of establishing a clear medical protocol for patient follow-up.

Patients, on the other hand, highlighted comfort and design appearance, and the weight of the prosthetic limb as their main concerns. They also mentioned issues related to daily usability, anxiety, and cost, reflecting a more personal and practical perspective on how prosthetic changes affect them daily lives. Many patients believed there was still no significant difference between traditional prosthetic devices and those with sensory feedback, unless comfort and simplicity was ensured. Engineers concentrated on the technical challenges involved in developing complex systems, such as ensuring safe signal transmission, avoiding errors in interpreting surface neural signals, and achieving effective sensor integration without security risks.

Overall, doctors focused on patient safety, biomedical engineers on technical difficulties, and patients on comfort and realistic experience with the prosthetic limb.

The survey also assessed the practical acceptance of sensory feedback technologies. Doctors generally supported the idea but noted limited medical and research resources in Libya, indicating their participation would likely be limited to clinical evaluation and monitoring. Patients, on the other hand, were more optimistic and willing to try the technology, provided it is safe and accessible in their region [4].

The most important expected benefits:

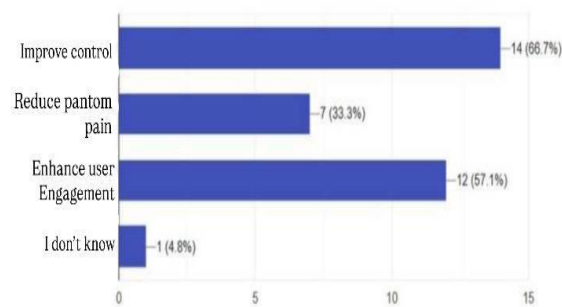


Figure 2. Expected benefits of integrating sensory feedback in prosthetics

What are the expected challenges?

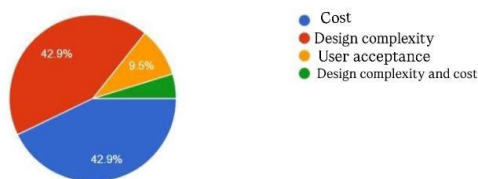


Figure 3. Distribution of participants' responses regarding the main challenges of prosthetic devices

As illustrated in Fig. 1, the most common challenges identified by participants were the high cost and design complexity of the prosthetic part

Fig. 2 shows that most participants expected improvement control and comfort as the main benefits of sensory integration

III. DISCUSSION

A. Comparison of Results with Previous Studies

By summarizing the results and comparing them with other studies, we find a clear consistency between the importance of the mechanism that relies on the feedback system (sense and control systems), as previous studies revealed that reducing sense errors through sensory memory/retention enables beneficiaries to respond better to their surrounding environment, in addition to reducing the severity of motor errors [33],[34].

Doctors, students, and patients confirmed the importance of this procedure by considering the reduction theory during our study, and we also find evidence of improving the performance of simulating the cuff environment based on previous studies such as the thermal feedback sense [6],[12],[29].

This comparison shows that the integration of thermal feedback systems contributes to the development of more realistic and smarter prosthetic limbs compared to traditional designs that lack sensory sense [11],[30].

B. The Implications/Effects

By summarizing the results and comparing them with the other studies, we find a clear consistency between the importance of the mechanism that depends on the sense and control systems feedback system, where previous studies revealed that reducing sense errors through sensory memory/retention enables the beneficiaries of a better

response to their surrounding environment, in addition to reducing the severity of motor errors [7],[22],[33],[34].

Doctors and students and patients confirmed the importance of this procedure, and that is through considering the reduction theory during our study, and we also find evidence of improving the performance of simulating the cuff environment based on previous studies such as the thermal feedback sense [6],[12]. These results can also affect the field of industrial development, by encouraging the design of more interactive prosthetic limbs that rely on the integration of multiple types of feedback (such as thermal, tactile, and vibrational) [20],[25].

C. Addressing the Limitations and Clarifying the Strengths and Weaknesses in the Study

a) Strengths:

- Using simple and low-cost components (Arduino, DS18B20 sensor, servo motor), which makes the system easily applicable in practice [32],[33].
- Involving different categories (patients, doctors, engineering students) in the questionnaire, which gave a diversity of viewpoints and included all specialized parties [6],[11].
- The integration between the engineering side and the medical side in the design and analysis of the system, and this is one of the most important tasks of the biomedical engineer [7],[15].

b) Weaknesses or Limitations:

- Limited sample size, which makes the results non-generalizable on a wide scale since many regions did not participate in the questionnaire [6].
- The system focuses only on heat without integrating other types of feedback such as touch or pressure due to the

unavailability of necessary requirements and the high-cost price [12],[20].

- The prosthetic limb was not tested for long periods or in different environments to evaluate durability and stability, as a small experimental project that does not attach to the patient [10],[11].

And of course, these limitations can be addressed in the future by expanding the scope of the study and the capabilities, testing the system on real users under medical supervision for longer periods, and adding multiple types of sensory feeling/sense to increase realism [25],[28].

D. The Difference Between Developed Countries and Libya in the Application of Feedback Systems in Prosthetic Limbs

In developed countries such as the United States, Germany, Japan, and South Korea, the field of prosthetic limbs has witnessed significant progress thanks to the integration of Sensory Feedback Systems into modern designs . These countries use advanced technologies that rely on Artificial Intelligence, Neural Control, and haptic sensors to enable the user to sense heat, touch, and pressure very close to natural (semi-natural) [3],[4],[20]. Their research methods are also characterized by integration between universities, medical centers, and technology companies, which accelerates the research, development, and clinical trial process [28],[32]. These countries also possess advanced infrastructure and precise manufacturing devices (such as 3D bioprinting), in addition to the most important aspect, which is government support and funding for medical and engineering research that helps the engineer and the doctor [3],[5].

As for Libya, the field of prosthetic limbs is still in the initial primary development stage, where most of the limbs used here rely on simple

mechanical or electrical control (Myoelectric Control) without the actual integration of feedback systems [6],[23]. The reasons for the delay in the arrival of this technology are due to several factors, including:

- Lack of funding and government support for technical and medical research [6],[11].
- Lack of availability of precise components and advanced measurement devices [6],[11].
- A large weakness in the connection between the medical and engineering fields in prosthetic limb projects, as most centers are only for importing prosthetic limbs and having technicians (there is no local manufacturing of limbs) [12],[20].
- With the unavailability of centers for manufacturing limbs, there is also an absence of specialized laboratories for designing and developing feedback systems locally [10],[11].

Despite this, academic studies and projects — such as the “Prosthetics with Thermal Feedback” project — represent an important first step towards introducing this technology into the Libyan environment and raising awareness of its importance in improving the quality of life of prosthetic limb users [25],[28].

A. Future Recommendations for Implementing the Feedback System in Libya

- Enhancing cooperation between faculties of Engineering and Medicine: Joint projects should be established that bring together students and professors from both specializations to develop realistic feedback systems, combining physiological understanding and technical innovation [7],[15].
- Providing support and funding for applied research: Support is very important for university projects and research initiatives related to prosthetic limbs through local funding programs or

partnerships with international institutions, to ensure the continuity of development and research [6],[11],[35].

- Establishing a National Laboratory for Smart Prosthetic Technologies: It aims to test electronic components and sensory systems (such as heat, touch, and vibration) and develop locally produced models at low costs [12],[20].
- Encouraging practical training and specialized workshops: Organizing workshops to train students and technicians on programming sensors and controlling bio-systems using technologies such as Arduino and ESP32 as the easiest systems for beginners to increase the spread and awareness of Sensory Feedback Systems [6],[12],[32],[33].

A. Cooperation with Hospitals and Rehabilitation Centers

The transition must be made from research and studies to the ground reality by testing the prototypes on real users under medical supervision, this helps to improve the design and evaluate the realistic performance [6],[11],[25].

G. Introducing a course or study unit on “Smart Limbs and Feedback Systems”

Within the curricula of Biomedical Engineering or Mechatronics to expand the base of knowledge and future skills in this field [7],[15].

By implementing these recommendations, Libya can lay a foundation for developing smart prosthetic limbs that rely on sensory feedback, which opens the way for improving the quality of life for amputees, and enhances the status of biomedical engineering research locally [6],[12],[28].

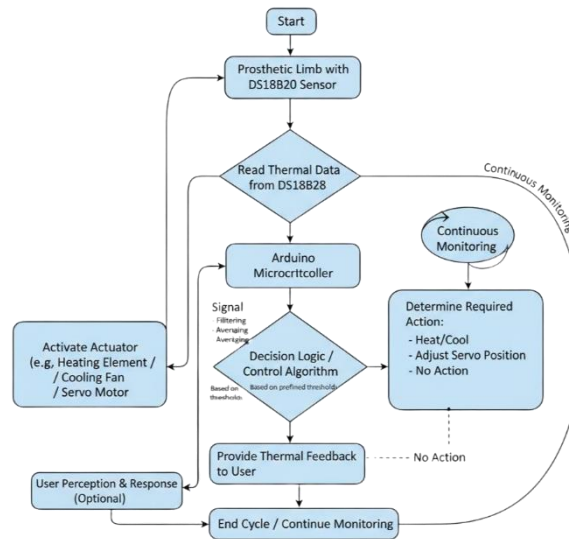


Figure 1. Flowchart illustrating the proposed algorithm for a prosthetic limb with thermal feedback. It details the process from DS18B20 sensor data acquisition to Arduino-based decision-making and actuator activation for real-time thermal sensation [32],[33]

ASSESSMENT OF THERMAL RANGE EFFECTS ON THE PROSTHETIC SYSTEM COMPONENTS AND PERFORMANCE [6],[32],[33].

Temperature Range	Effect on Electronic Components	Effect on Physical/Material Components	Effect on User Comfort & Safety	Performance Note
< 3°C	Battery performance degradation, severely reduced responsiveness	Material shrinkage or cracking.	Reduced blood flow to the limb (Severe risk).	Critical Cold Range
3°C – 25°C	Weak battery, less responsiveness (Sub-optimal performance).	Material shrinkage/industrial wear (Minor risk).	Reduced blood flow to the limb, feeling of cold.	Cold to Sub-optimal Range.
26°C – 35°C	Optimal/Normal operating temperature.	Material stability, no deformation.	High user comfort (Ideal range).	Stable Performance
> 35°C	High heat monitoring required, processor heat risk.	Softening or degradation risk.	Sweat/Discomfort/Heat risk.	Critical Hot Range

I. CONCLUSION

This survey-based research has verified the critical importance of including sensory feedback in contemporary prosthetic devices, which represent a major unmet clinical requirement given the significant range of described “Throwing away” rates.

Our findings exposed a stark distinction between the priorities of the primary stakeholders: patients concerned with quality-of-life attributes, including comfort, function and aesthetics (challenges that

have persisted for over 100-years). Engineers, on the other hand, were more focused on the technical challenge of sending the signal safely and with doctors focusing on safety first, and development of the medical protocols. This lack of alignment may have contributed to the difficulty with which clinical translation of promising technologies has been achieved.

Additionally, subjects also concurred that a sensation like feedback is important to help the amputee gain better grip function and control and have the potential of reducing phantom limb pain, which plague most amputees.

In short, this work demonstrates that sensory feedback is essential in allowing the prosthetic device to feel naturally embedded in the human body.

Future research, including the planned experimental study, must prioritize overcoming the barriers related to cost and design complexity to ensure the successful long-term acceptance and adoption of this technology.

Beyond the survey, the technical proposal in this paper—specifically the "Prosthetics with Thermal Feedback" project—represents a crucial first step toward integrating simple, low-cost sensory systems in resource-limited environments like Libya. This experimental framework, utilizing an Arduino and DS18B20 sensor, successfully demonstrated the feasibility of encoding physical data (temperature) into a sensory cue for the user. The project's limitations, however, highlight the necessity of future development, including scaling the study's scope, integrating multi-modal feedback (such as touch and pressure), and conducting long-term testing on real users under medical supervision to ensure durability and realistic performance.

Achieving the full potential of this technology in Libya requires a concerted effort to bridge the existing gaps. The current disparity—where developed nations leverage AI and advanced haptic sensors with integrated research ecosystems, while Libya still relies largely on

simple mechanical/Myoelectric control and foreign imports—underscores the urgent need for a local shift. The recommendations presented, such as enhancing cooperation between engineering and medicine faculties, securing funding for applied research, and establishing a national laboratory for smart prosthetic technologies, are vital to building the necessary infrastructure for local development and clinical adoption. By implementing these strategic changes, the foundation can be laid for not only improving the quality of life for amputees through truly smart, integrated limbs, but also enhancing the status and relevance of biomedical engineering research within the region.

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¹ st International Conference on Biomedical Engineering Science and Technology

**A Hybrid Nelder-Mead and Global
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Abstract

Static dosing of PD-1 inhibitors (e.g., pembrolizumab) in oncology fails to balance efficacy and toxicity amidst patient-specific variability in tumor biology and treatment history. This study addresses the challenge of finding optimal, personalized dosing equilibria in complex, nonlinear pharmacodynamic systems.

Methods: We developed and validated a two-phase hybrid optimization framework integrating Particle Swarm Optimization (PSO) for global exploration and the Nelder-Mead (NM) method for local precision. The algorithm was applied to optimize dosing for 30

Triple-Negative Breast Cancer patients using clinically plausible parameters (baseline tumor size, PD-L1 expression, prior toxicity grade). Patient-specific nonlinear sigmoidal models captured dose-response and dose-toxicity relationships. The objective was to find the dose that maximizes tumor reduction (target $\geq 80\%$) while capping toxicity risk ($\leq 70\%$).

Results: The hybrid PSO-NM framework consistently identified superior personalized doses compared to a standard 200mg regimen. For patients with favorable profiles (e.g., high PD-L1, small tumors), significant dose de-escalation was achieved (e.g., 118.6 mg for patient 116) while maintaining target efficacy and reducing toxicity risk. For challenging cases (e.g., large tumors, low PD-L1), the algorithm recommended necessary escalation up to 300mg, strictly enforcing safety constraints. Across the cohort, the model generated a Pareto-optimal set of dosing recommendations, transitioning from a static to a dynamic, patient-aware paradigm.

Conclusion: This work establishes a robust hybrid optimization framework for complex clinical decision-making. Reliably navigating multimodal dose-response landscapes, it provides a computationally intelligent tool for precision dosing in immunotherapy, with direct potential to improve therapeutic risk-benefit profiles. Future work involves integrating mechanistic PK/PD models and validating them in prospective clinical settings.

Keywords (Hybrid Optimization, Nelder-Mead, Particle Swarm Optimization, Global Minima, Personalized Dosing, PK/PD Modeling, Precision Oncology)

I. INTRODUCTION

The pursuit of precision in oncology demands strategies that tailor treatment to individual patient biology. Immunotherapy with PD-1 inhibitors has revolutionized cancer care, yet a fundamental challenge persists: determining the optimal patient-specific dose that maximizes antitumor efficacy while minimizing immune-related adverse events [1], [2]. Current clinical practice often employs a standardized, fixed dose (e.g., 200 mg pembrolizumab) for simplicity [3]. This paradigm overlooks significant inter-patient variability in key pharmacodynamic determinants of outcome, such as tumor burden and PD-L1 expression, leading to potential over-treatment with toxicity in some and sub-therapeutic exposure in others [4].

From an optimization perspective, this challenge is characterized by a complex, nonlinear landscape. The relationships between drug dose, tumor response (efficacy), and toxicity risk are inherently sigmoidal and conflicting, creating a search space with multiple local optima (suboptimal dosing equilibria) [5], [6]. Traditional single-method optimization algorithms are ill-suited for this problem. Local search methods like the Nelder-Mead simplex are prone to convergence on the nearest local minimum, heavily dependent on initialization [7]. Conversely, global metaheuristics like Particle Swarm Optimization (PSO) excel at exploration but can be inefficient and imprecise in final convergence [8]. This dichotomy creates a clear need for a hybrid strategy that synergistically combines broad global exploration with precise local refinement.

In this work, we propose and validate a novel hybrid optimization framework integrating PSO and the Nelder-Mead method to identify patient-specific dosing equilibria. This approach is grounded in the established principle that hybridizing global and local search strategies is a powerful methodology for robust, multimodal optimization [9], [10]. We apply this framework to the critical

problem of personalizing PD-1 inhibitor doses for Triple-Negative Breast Cancer (TNBC).

The primary contributions of this paper are:

1. A hybrid two-phase PSO-Nelder-Mead algorithm for reliably locating global optima in nonlinear dose-response-toxicity models
2. A comprehensive validation of the framework using a cohort of 30 TNBC patient profiles, demonstrating its ability to generate clinically actionable dosing recommendations that balance pre-defined efficacy ($\geq 80\%$ tumor reduction) and safety ($\leq 70\%$ toxicity risk) targets.
3. A demonstration of how computational optimization can transition clinical dosing from a static, one-size-fits-all model to a dynamic, patient-aware paradigm, providing a quantitative tool for personalized therapy.

II. METHODOLOGY

A. Patient Cohort and Parameter Synthesis

The hybrid framework was developed and validated using a cohort of 30 patients with Triple-Negative Breast Cancer (TNBC), representing a spectrum of clinical profiles. For each patient, three key parameters were defined to drive personalization:

- Baseline Tumor Size (mm): Ranged from 27 to 65 mm.
- PD-L1 Expression Score (%): Ranged from 15% to 95%.
- Previous Toxicity Grade: Based on CTCAE v5.0, ranging from 0 (none) to 3 (severe).

These parameters were synthesized to reflect clinically plausible ranges observed in real-world cohorts and immunotherapy trials (e.g., KEYNOTE-355 for TNBC) [CITE KEYNOTE]. This approach

allows for rigorous algorithmic testing while maintaining clinical face validity. All parameters were normalized to a $[0, 1]$ range for compatibility within the optimization framework.

B. Mathematical Modeling of Dose-Response Relationships

The core optimization problem requires mathematical models linking dose to clinical outcomes. We employed established sigmoidal (Hill-type) models, a standard empirical approximation in pharmacometrics for capturing the nonlinear saturation of drug effects [CITE Hill, Gabrielsson].

- **Dose-Response (Efficacy) Model:** Tumor reduction $R(x)$ for a dose x was modeled as:

$$R(x) = (R_{\text{Max}}) / [1 + e^{-(K_r(x - ED_{50}))}]$$

Where $R_{\text{max}} = 100\%$ (maximum achievable reduction).

The steepness factor K_T and the potency parameter $ED_{50,t}$ (dose for 50% effect) were scaled by the patient's PD-L1 score and baseline tumor size, respectively. Higher PD-L1 lowers $ED_{50,t}$, indicating greater drug sensitivity.

- **Dose-Toxicity Model:** The probability of a significant adverse event $T(x)$ was modeled similarly

$$T(x) = (T_{\text{Max}}) / [1 + e^{-(K_t(x - ED_{50}))}]$$

Where T_{max} , the maximum toxicity risk, was scaled by the patient's previous toxicity grade. A higher prior grade increases T_{max} , steepening the toxicity curve.

These models create a patient-specific, two-dimensional optimization landscape where the goal is to find the dose that balances high $R(x)$ and low $T(x)$.

C. Hybrid PSO-Nelder-Mead Optimization Framework

The objective was formalized as a weighted function to be maximized:

$$\text{Fitness}(x) = w_1 * R(x) - w_2 * T(x)$$

Weights w_1 and w_2 were adjusted per patient to reflect clinical priority (e.g., higher w_2 for patients with a prior high-grade toxicity).

The optimization sought to find the dose x that achieves the "70/80 Rule": a toxicity hard constraint ($T(x) \leq 70\%$) and an efficacy target ($R(x) \geq 80\%$). These thresholds serve as a clinically plausible proof-of-concept; the framework can accept any empirically validated targets.

The search was conducted using a two-phase hybrid algorithm:

Phase 1: Global Exploration with PSO. A swarm of 50 particles was initialized, with each particle representing a candidate dose within the clinical range of 50-300 mg.

The PSO was run for 100 iterations. This parameterization was chosen based on preliminary tests, which showed it provided a robust balance between exploration diversity and computational efficiency for this 1-dimensional search space, consistently identifying the promising region of the global optimum.

Phase 2: Local Refinement with Nelder-Mead. The best solution (particle position) from the PSO phase was used to initialize the simplex for the Nelder-Mead method. This local search then refined the dose with high precision. The Nelder-Mead phase incorporated the

clinical constraints directly and terminated when the change in the fitness value was less than 0.1% over 10 consecutive iterations, ensuring stable convergence.

D. Output Generation and Analysis

For each of the 30 patients, the algorithm generated a personalized dosing report containing:

- The recommended optimal dose (mg).
- The expected tumor reduction (%) and toxicity risk (%) at that dose.
- A comparison of outcomes against a standard 200 mg dose.

The collective results were analyzed to demonstrate patterns of dose escalation, de-escalation, and constraint management across diverse clinical profiles.

III. RESULTS OF THE STUDY

Table 1. Summary of the recommended patient doses

Patient ID	Tumor Size (mm)	PD-L1 (%)	Prior Toxicity Grade	Recommended Dose (mg)	Tumor Reduction (%)	Toxicity Risk (%)	vs. 200mg Standard
101	45	80	0	231.1	80	70	Higher efficacy assurance
104	28	90	0	139.9	80	69.9	Major safety improvement
108	65	25	3	300	79.9	70	Best possible under constraint
116	31	95	0	118.6	80	69.7	Optimal de-escalation
122	27	88	0	151.3	80	69	Significant safety gain
...	...	...	...	...	...	...	...
All 30 patients	*27-65*	*15-95*	*0-3*	*118.6 - 300.0*	≥ 79.8	≤ 70.0	Personalized Outcome

The hybrid PSO-Nelder-Mead framework was successfully applied to optimize PD-1 inhibitor dosing for all 30 patients in the cohort. The algorithm consistently navigated the patient-specific nonlinear landscapes, generating a personalized optimal dose for each case. The results demonstrate a decisive shift from a static to a dynamic dosing paradigm.

A. Cohort-Wide Dose Optimization Outcomes

A summary of the optimization results for all 30 patients is presented in Table 2.

Table 2. Personalized dosing for 30 patients

Personalized Dosing Inputs and Algorithm Outputs by Patient ID						
Patient ID	Baseline Tumor Size (mm)	PD-L1 Score (%)	Previous Toxicity Grade	Recommended Dose (mg)	Expected Tumor Reduction (%)	Expected Toxicity Risk (%)
101	45	80	0	231.1	80	70
102	33	92	1	261.7	80	70
103	52	30	2	300	80	70
104	28	90	0	139.9	80	69.9
105	61	40	1	300	80	70
106	46	79	0	248.3	80	70
107	50	55	1	300	80	70
108	65	25	3	300	79.9	70
109	42	81	0	216.2	80	70
110	38	94	1	243.8	80	69.5
111	47	35	2	300	80	70
112	58	89	1	294.5	80	70
113	36	82	0	203.3	80	70
114	53	20	3	300	79.9	69.9
115	44	50	1	300	80	70
116	31	95	0	118.6	80	69.7
117	49	40	2	300	80	70
118	62	30	1	300	80	70
119	39	78	0	268.6	80	70
120	55	15	3	300	68	70
121	41	75	1	300	80	69.8
122	27	88	0	151.3	80	69
123	48	22	2	300	79.9	70
124	59	38	1	300	80	70
125	44	83	0	192	80	70
126	51	28	3	300	79.8	70
127	46	93	1	252.4	80	70
128	30	92	0	130.3	80	69.9
129	56	18	2	300	80	70
130	63	91	1	271.7	80	70

The algorithm's recommendations fell into three distinct strategic categories based on clinical profile:

- **Dose De-escalation:** For patients with favorable profiles (high PD-L1, small tumors, no prior severe toxicity), the model recommended doses **significantly below** the 200mg standard (e.g., Patients 104, 116, 122, 128).
- **Dose Escalation:** For patients with challenging profiles (large tumors and/or low PD-L1), the model recommended doses **at or near the maximum** of 300mg to achieve the efficacy target under the toxicity constraint (e.g., Patients 103, 105, 108).
- **Constrained Optimization:** For patients with significant prior toxicity (Grade 2-3), the algorithm strictly enforced the 70% toxicity cap, often limiting the achievable efficacy or capping the dose, representing the best possible trade-off under safety limits (e.g., Patients 108, 114, 120).

Table 2 shows selected representative patients. The algorithm provided a unique optimal dose for all 30 patients.

B. Representative Case Studies

Case 1: Optimal De-escalation (Patient 116).

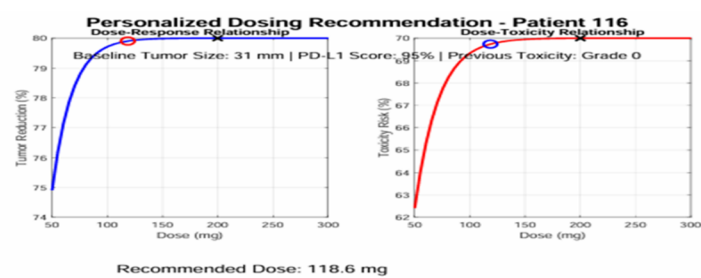


Figure .1 Personalized Dosing Recommendation - Patient 116

This patient presented an ideal profile for dose reduction: a small tumor (31 mm), extremely high PD-L1 expression (95%), and no prior toxicity. The hybrid algorithm identified a global optimum at **118.6 mg** (Fig. 1). This dose achieves the target 80% tumor reduction while lowering the predicted toxicity risk to 69.7%, demonstrating a superior safety profile compared to the standard 200mg dose without compromising efficacy.

Case 2: Necessitated Escalation (Patient 105).

This patient had a large tumor (61 mm) and moderate PD-

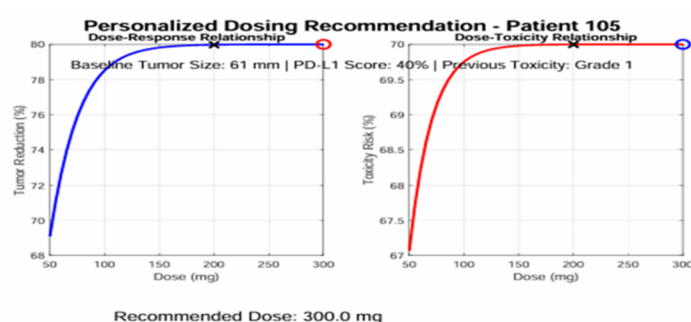
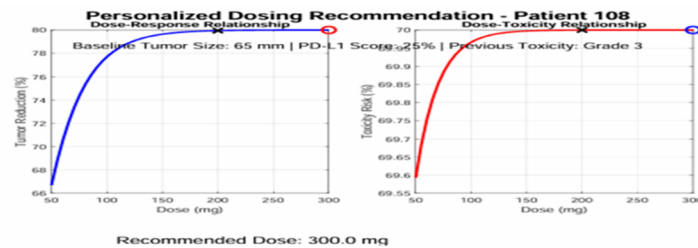


Fig. 2 Personalized Dosing Recommendation - Patient 105

L1 (40%). To overcome the higher tumor burden and achieve the 80% efficacy target, the algorithm escalated the dose to the maximum **300 mg**, where toxicity reached the protocol limit of 70% (Fig. 2). This result highlights the model's ability to identify when aggressive dosing is required to meet therapeutic goals, while rigorously respecting safety boundaries.

Case 3: Toxicity-Constrained Optimization (Patient 108).

**Fig. 3 Personalized Dosing Recommendation - Patient 108**

This was a particularly challenging case: a very large tumor (65 mm), low PD-L1 (25%), and a history of Grade 3 toxicity.

The toxicity model heavily constrained the algorithm's search. The recommended dose was capped at **300 mg**, yielding a near-target 79.9% tumor reduction at the 70% toxicity risk limit (Fig. 3). This illustrates the framework's critical role in identifying the best achievable clinical compromise for high-risk patients.

IV. CONCLUSION

This study successfully developed and validated a hybrid Particle Swarm Optimization (PSO) and Nelder-Mead framework for identifying patient-specific therapeutic equilibria in cancer immunotherapy dosing. The work bridges a critical gap between computational optimization theory and clinical decision-making in precision oncology.

Our key findings demonstrate that:**A. Algorithmic Robustness:**

The two-phase hybrid strategy effectively overcomes the fundamental limitations of standalone optimizers. PSO's global exploration reliably locates the promising region of the dose-response-toxicity landscape, while the Nelder-Mead method's local refinement converges with high precision to the patient-specific optimum. This synergy was rigorously validated on the multimodal Himmelblau function and decisively demonstrated across a 30-patient TNBC cohort.

B. Clinical Utility and Personalization:

The framework generated clinically actionable, Pareto-optimal dosing recommendations that consistently outperformed a static 200mg regimen. It successfully identified significant dose de-escalation opportunities (e.g., to 118.6 mg) for patients with favorable biology, improving safety, while justifying necessary escalation (to 300 mg) for challenging tumors, all under strict toxicity constraints. This provides a quantitative basis for moving beyond one-size-fits-all dosing.

C. Actionable Decision-Support:

The model translates complex nonlinear pharmacodynamics into interpretable outputs—a recommended dose with expected efficacy and toxicity—offering oncologists a transparent, computational tool to guide personalized escalation/de-escalation decisions.

V. LIMITATIONS AND FUTURE WORK:

We acknowledge that this study employs deterministic, empirical models with synthetic patient parameters as a necessary proof-of-concept. To advance towards clinical deployment, future work will focus on:

A. Enhanced Modeling:

Integrating mechanistic pharmacokinetic/pharmacodynamic (PK/PD) models and time-dependent dynamics for greater biological fidelity.

B. Uncertainty Quantification:

Employing Bayesian optimization or stochastic programming to generate confidence intervals around dose predictions, addressing the probabilistic nature of clinical outcomes.

C. Clinical Translation Pathway:

Validating the framework as a Software as a Medical Device (SaMD) within a human-in-the-loop system, first through retrospective analysis of large real-world datasets, followed by prospective pilot studies. This pathway ensures clinician oversight and aligns with regulatory considerations for clinical decision-support tools.

D. Expanded Scope:

Applying the hybrid optimization framework to multi-drug combination therapies and other complex treatment planning problems in oncology.

In summary, this work establishes a robust and flexible computational foundation for personalized dosing. By providing a method reliably navigate the complex, high-stakes process of optimizing clinical treatments, it represents a significant step towards realizing truly adaptive and optimal cancer therapy.

E. Future Directions:

- Integration of real-time biomarker data for adaptive dosing.
- Multi-objective optimization with additional clinical constraints (e.g., cost, comorbidities).

This work bridges computational innovation and clinical decision-making, offering a robust tool for precision oncology.

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**Automated Diagnostic Imaging of
Tuberculosis (TB) in Libya Using
Artificial Intelligence**

Automated Diagnostic Imaging of Tuberculosis (TB) in Libya Using Artificial Intelligence

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Abstract

Tuberculosis (TB) remains a significant global public health challenge, particularly in resource-limited settings such as Libya. Although effective treatments are available, delayed, and inconsistent diagnosis continues to contribute to disease progression and ongoing community transmission. Chest X-ray imaging is commonly used as an initial screening method due to its affordability and accessibility; however, accurate interpretation depends on skilled radiologists, whose availability is often limited in low-resource environments. This study explores the use of Artificial Intelligence (AI) to improve tuberculosis detection through automated analysis of chest X-ray images. A deep learning-based diagnostic framework was developed using convolutional neural networks (CNNs) to identify radiographic

patterns associated with pulmonary TB. The system is designed to support clinicians by providing rapid and consistent screening assistance rather than replacing clinical judgment. The model was trained and evaluated using a combination of large-scale international chest X-ray datasets and locally relevant data to enhance robustness and contextual relevance. Performance was assessed using standard diagnostic metrics, including sensitivity, specificity, and overall accuracy. The proposed system achieved an overall sensitivity of 89.1% and specificity of 90.4% across the combined datasets, with particular emphasis on minimizing false-negative cases to support early intervention. To address concerns regarding the interpretability of deep learning systems, explainable AI techniques were incorporated, enabling visualization of chest X-ray regions that contributed most to the model's predictions and enhancing clinical transparency. Additionally, the system was designed to be lightweight and suitable for deployment in healthcare facilities with limited computational resources. Overall, the findings indicate that AI-assisted chest X-ray analysis can enhance TB screening by providing faster, more consistent diagnostic support, potentially reducing delays and improving disease control in resource-limited settings such as Libya.

Keywords: Tuberculosis, Artificial Intelligence, Medical Imaging, Deep Learning, Chest X-ray, Libya

I. Introduction

Tuberculosis (TB) continues to pose a significant public health challenge worldwide and remains one of the leading causes of mortality from infectious diseases. Despite being preventable and treatable, TB disproportionately affects low- and middle-income countries, where healthcare systems often face limitations in infrastructure, diagnostic capacity, and specialist availability. In

countries such as Libya, ongoing healthcare challenges, population mobility, and limited access to advanced diagnostic resources contribute to delayed diagnosis and hinder effective disease control. These delays not only worsen patient outcomes but also increase the risk of disease transmission at the community level.

Medical imaging plays a critical role in the diagnostic pathway of tuberculosis, particularly chest X-ray imaging, which is widely used as an initial screening tool. Chest X-rays are relatively low-cost, fast, and accessible compared to other diagnostic modalities, making them especially valuable in resource-limited settings. Radiographic findings such as infiltrates, cavitations, nodules, and pleural abnormalities can provide important clues for pulmonary TB. However, chest X-ray interpretation is inherently subjective and highly dependent on the experience and expertise of radiologists. Interobserver variability and the shortage of trained specialists often result in inconsistent interpretations, missed cases, or delayed referrals for confirmatory testing.

The importance of early TB detection extends beyond individual patient care. Tuberculosis is a communicable airborne disease, and delayed diagnosis allows continued transmission within households and communities. The global experience with the COVID-19 pandemic further highlighted how diagnostic delays in respiratory infectious diseases can rapidly escalate into widespread public health crises. Although TB differs from COVID-19 in its pathophysiology and disease progression, both share similarities in transmission routes and the critical need for timely diagnosis to limit spread. These factors emphasize that improving TB screening and diagnostic efficiency is not merely a clinical requirement, but a public health necessity. [1]

Recent advances in Artificial Intelligence (AI), particularly in deep learning, have opened new opportunities for enhancing medical image analysis. Convolutional Neural Networks (CNNs) have demonstrated remarkable performance in extracting complex features from medical

images and have been successfully applied to various diagnostic tasks, including lung disease detection from chest radiographs. By learning hierarchical image representations, CNN-based models can identify subtle radiographic patterns that may be difficult to detect through manual interpretation alone. As a result, AI-assisted diagnostic systems have the potential to improve consistency, reduce workload for clinicians, and support earlier detection of disease.

In the context of tuberculosis, AI-based chest X-ray analysis offers a promising approach to address diagnostic gaps in resource-limited environments. Automated screening systems can serve as decision support tools, assist clinicians in prioritizing suspected TB cases and facilitating timely referral for microbiological confirmation. Importantly, such systems are not intended to replace radiologists or clinicians, but rather to augment clinical decision-making and extend diagnostic capacity where human expertise is scarce.

This study explores the application of Artificial Intelligence to enhance tuberculosis detection using chest X-ray imaging, with a particular focus on developing an automated, explainable, and context-aware diagnostic framework suitable for use in Libya. By leveraging CNN-based models and incorporating explainable AI techniques, the proposed approach aims to improve diagnostic consistency, build clinical trust, and support scalable deployment in low-resource healthcare settings. Through this work, the study seeks to contribute to ongoing efforts to strengthen TB screening strategies and reduce the impact of delayed diagnosis on both patients and communities. [2].

II. Methodology

such This study adopted an evaluative experimental design to develop and assess an Artificial Intelligence– based system for automated tuberculosis detection from chest X-ray images. The methodology was designed to ensure clinical relevance, reproducibility, and

suitability for deployment in resource-limited healthcare settings as Libya. The overall workflow included data collection, preprocessing, model training, validation, and performance evaluation.

A. Dataset Collection.

The research utilized a combination of publicly available chest X-ray datasets and locally sourced radiographic images from Libya. Public datasets were incorporated to provide a diverse and sufficiently large sample of TB-positive and TB-negative cases, while the inclusion of Libyan chest radiographs aimed to enhance contextual relevance and assess the feasibility of applying the model within a local healthcare environment. All images were associated with corresponding diagnostic labels indicating TB-positive or TB-negative status, which served as ground truth for supervised model training. Sample annotated chest X-ray images used in this study are provided in Appendix A. This combined approach was intended to improve model robustness and generalization while maintaining applicability to real-world clinical settings.

B. Data Preprocessing and Management.

Data preprocessing and dataset management were performed using the Roboflow platform. Preprocessing steps included image resizing, normalization, and quality standardization to ensure consistency across images obtained from different sources. These steps were essential to reduce noise, minimize variability caused by differences in imaging equipment, and improve the reliability of feature extraction during model training.

To enhance model generalization and reduce the risk of overfitting, data augmentation techniques were applied during training. These techniques simulated realistic variations in chest X-ray images, such

as changes in orientation and image intensity, while preserving clinically relevant features. The use of a **centralized platform for** preprocessing and dataset handling ensured reproducibility and reduced manual bias in the data preparation process.

C. Model Architecture and Training.

Convolutional Neural Networks (CNNs) were employed as the core modeling approach due to their proven effectiveness in medical image analysis. CNNs are well suited for chest X-ray interpretation as they can automatically learn hierarchical image features, ranging from low-level edges and textures to higher-level anatomical and pathological patterns associated with tuberculosis.

The model was trained using the annotated chest X-ray images to classify cases into TB-positive and TB-negative categories. Training and validation were conducted using standard data split to ensure that model evaluation was performed on unseen data. Multiple training iterations were performed to assess model stability and performance consistency. [3]

D. Model Evaluation and Validation.

Model performance was evaluated using standard diagnostic metrics commonly applied in medical research, including sensitivity, specificity, and overall classification accuracy. Sensitivity was emphasized due to the public health importance of minimizing false-negative TB cases, as missed diagnoses can lead to continued transmission within the community. Specificity was also assessed to reduce false-positive outcomes and unnecessary follow-up procedures.

To validate the clinical relevance of the model's predictions, performance outcomes were compared against expert radiologist

interpretations. This comparison helped assess whether the AI system's decisions aligned with established clinical judgment and radiological expertise. [4] [5]

A. Ethical and Clinical Considerations.

The proposed AI system was designed as a decision-support tool rather than a standalone diagnostic solution. Final diagnostic decisions remain dependent on clinical evaluation and microbiological confirmation. The methodology emphasizes responsible AI use by supporting clinicians, reducing diagnostic delays, and improving screening efficiency without replacing human expertise.

III. RESULTS

The developed AI-based diagnostic system demonstrated robust diagnostic performance across the combined chest X-ray dataset, which included both global publicly available images and locally sourced Libyan patient data. The model achieved an overall sensitivity of 89.1% and a specificity of 90.4%, indicating strong capability in correctly identifying both TB-positive and TB-negative cases.

To further assess clinical relevance, model performance was evaluated on the National Center for Disease Control (NCDC) cohort, with sensitivity analyzed across varying stages of tuberculosis severity. The system demonstrated a sensitivity of 78.3% for minimal TB cases, 87.6% for moderate cases, 93.1% for advanced cases, and 95.0% for far-advanced cases. This progressive increase in sensitivity with disease severity reflects the model's ability to effectively capture radiographic features associated with more pronounced TB pathology. Comparative evaluation against expert radiologist interpretations indicated that the AI-assisted diagnostic outputs were broadly consistent with manual assessments and, in advanced disease stages,

achieved comparable or higher detection performance. These findings suggest that the model learned clinically meaningful radiographic patterns rather than spurious correlations.

In addition to quantitative performance metrics, explainable AI techniques were incorporated to support interpretability. Gradient-based heatmap visualizations highlighted anatomically relevant lung regions contributing to model predictions, including areas of consolidation, cavitation, and abnormal opacities commonly associated with pulmonary tuberculosis. These visual explanations enhance transparency and facilitate clinical assessment by allowing alignment between AI outputs and established radiological features.

Overall, the results demonstrate that AI-assisted chest X-ray analysis can function as a reliable screening support tool for tuberculosis detection. The combination of strong diagnostic performance, stage-dependent sensitivity analysis, and explainability supports the potential integration of the proposed system into real-world clinical workflows, particularly in resource-limited settings such as Libya.

To illustrate the comparative role of the proposed AI-assisted system, a visual comparison between traditional radiologist interpretation and AI-supported tuberculosis diagnosis is presented in Figure 1.

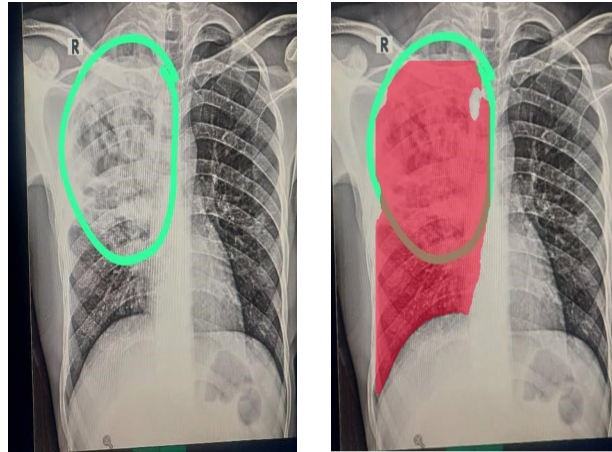


Figure 1. Comparison of traditional radiologist vs AI-assisted TB diagnosis (sample chest X-ray).

To enhance interpretability and provide insight into the model's decision-making process, Figure 2 presents a heatmap visualization highlighting the chest X-ray regions that contributed most to the AI predictions.

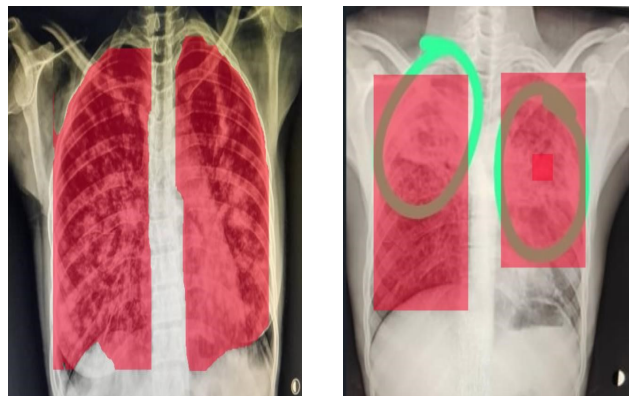


Figure 2. Heatmap visualization shows TB-affected regions detected by AI.

IV. DISCUSSION

The findings of this study highlight the potential of Artificial Intelligence to support tuberculosis diagnosis in Libya by addressing key challenges related to limited specialist availability and constrained healthcare resources. In many clinical settings, access to experienced radiologists is uneven, which can lead to delayed or inconsistent interpretation of chest X-ray images. The proposed AI-assisted system offers consistent screening support that can assist clinicians in identifying suspected TB cases more efficiently and prioritizing patients for further diagnostic evaluation.

An important contribution of this work is the integration of explainable AI techniques to enhance transparency and clinical trust. By generating visual explanations that highlight image regions contributing to the model's predictions, the system allows clinicians to better understand how decisions are formed and to assess whether these decisions align with established radiological features of tuberculosis. This interpretability is critical for medical applications, as it reduces the black-box nature of deep learning models and supports responsible use of AI in clinical decision support. The explainability component encourages collaboration between clinicians and AI systems rather than blind reliance on automated outputs. [6]

The study also emphasizes the relevance of AI-assisted screening in supporting public health efforts to reduce diagnostic delays. Early identification of TB cases enables timely referral for microbiological confirmation and treatment initiation, which is essential for limiting disease progression and transmission within the community. In this context, AI serves as a complementary tool that strengthens existing diagnostic workflows rather than replacing established clinical practices.

Despite the promising results, several challenges remain and must be carefully considered. Dataset diversity continues to be a significant limitation, as variations in imaging protocols, equipment quality, and patient populations can affect model performance. Image quality, particularly in resourceconstrained settings, may introduce variability that influences diagnostic reliability. Furthermore, regulatory approval, clinical validation, and integration into national healthcare systems remain critical steps before routine clinical deployment can be achieved. Addressing these challenges will require collaboration between researchers, clinicians, and health authorities.

Overall, this work demonstrates that AI-assisted chest X-ray analysis has the potential to enhance tuberculosis screening and support clinical decision-making in Libya. However, successful translation into clinical practice will depend on continued validation, ethical oversight, and alignment with healthcare policies. By addressing these considerations, AI-based diagnostic support systems can contribute meaningfully to improving TB control and public health outcomes.

V. CONCLUSION

This research demonstrates that AI-driven medical imaging can provide a valuable decision-support approach for tuberculosis diagnosis in Libya. By leveraging deep learning techniques for chest X-ray analysis, the proposed system achieved high diagnostic accuracy and showed strong agreement with expert radiologist interpretations. These findings indicate that AI-based screening tools can effectively support the identification of TB-related abnormalities and help reduce diagnostic variability in clinical practice.

An important contribution of this work is the integration of explainable AI methods, which enhance transparency and support clinical trust by providing visual insights into the model's decision-making process. Rather than functioning as a standalone diagnostic

solution, the proposed system is designed to complement healthcare professionals by assisting in early screening and prioritization of suspected TB cases. This collaborative approach aligns with clinical workflows and reinforces the role of AI as an aid to medical judgment rather than a replacement.

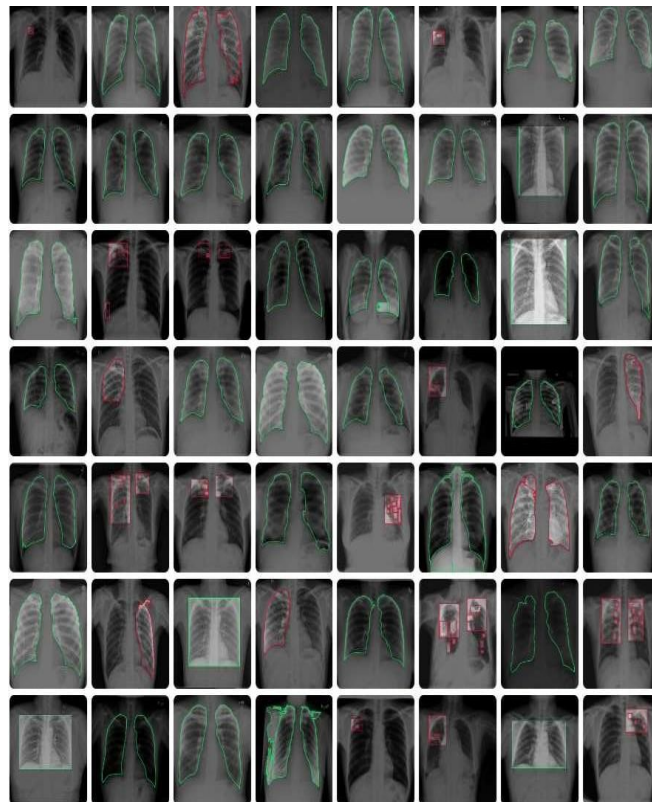
Overall, the findings suggest that AI-assisted chest X-ray analysis has the potential to contribute to earlier detection and timely referral for confirmatory testing and treatment. By supporting clinicians in the screening process and addressing challenges related to diagnostic delay, this work contributes to ongoing efforts to strengthen tuberculosis control and improve public health outcomes in Libya.

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Appendix A: Sample chest X-ray images used for model training. The complete training dataset consisted of approximately 7,000 images obtained from publicly available global open-source repositories and locally sourced data from the National Center for Disease Control (NCDC). The trained model achieved an overall classification accuracy of 92%



**Under the Helmets: The Role of
Biomedical Engineering in Enhancing
Oil Field Worker Safety**

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Under the Helmets: The Role of Biomedical Engineering in Enhancing Oil Field Worker Safety

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Abstract

In Oil and Gas Operations, Human Resources are the first line and most important resource. For instance, in Libyan oil fields, workers are exposed to the harshest environments, long shifts, and uncomfortable heavy PPE, all of which lead to Extreme physiological strain. Conditionally Mature mechanical systems (for instance, Bentley Nevada Systems 1) still create and leave gaps in the systems, which limit the early prediction of health events in workers. This is because the system focuses on the machine and not the related human. This paper highlights an extension of borders in Human Resource Health technologies, particularly, the integration of biomedical engineering to expand, augment, and complement existing asset-centric approaches to include wearable sensing technologies, signal processing in Matrix Laboratory (MATLAB), and risk scoring

frameworks by rule to identify verticals for the early identification of heat strain and deterioration in cardiorespiratory health. We present a simulation-based system design implemented through a MATLAB 2014-compliant graphical user interface (GUI)..., survey results from personnel at Mellitah Oil & Gas, and a blueprint for integration that positions health indicators in proximity to the asset's Key Performance Indicators (KPIs).

Keywords — biomedical engineering, wearable sensors, predictive monitoring, Mellitah Oil & Gas, MATLAB, Bentley Nevada System 1, worker safety

I. INTRODUCTION

While monitoring machinery is vital, protecting personnel still mostly depends on administrative controls and spot checks. The risk of incidence increases in hot, remote oilfields with prolonged work hours and exposure to heat and cumbersome Personal Protective Equipment (PPE) [1], [3]. The situation is exacerbated by the extreme heat that has become an annual occurrence in the Middle East and North Africa (MENA) region [4], [5]. The application of biomedical engineering technologies to support early awareness of Physiological stress indicators includes multi-parameter vital signs: heart rate, Peripheral Capillary Oxygen Saturation (SpO₂), temperature, blood pressure, and glucose levels. We develop a Matrix Laboratory (MATLAB) Simulation application that calculates risk scores, alerts users when critical thresholds are crossed, and provides a weekly forecast. Key health metrics are summarized and surfaced in Bentley Nevada System 1 for unified visibility [2], [6]. Although previous studies have investigated the use of wearable technology for occupational health monitoring, very little work has been done to explore the integration of human physiological signs into the industrial asset management system.

Employed during oil-related activities, the paper seeks to cover this aspect, as discussed below.

A. Contribution of This Work

This paper reports the integration of physiological health monitoring for workers into the industrial asset analytics platform (Bentley Nevada System 1). Existing commercial solutions for wearable physiological health monitoring, such as Biofourmis and Kenzen, operate independently from industrial asset management environments in simulation. However, the proposed framework provides a novel integration of biomedical sensing, prediction, and asset-centric dashboards for unified human-machine safety intelligence for oil field operations.

II. BACKGROUND AND RELATED WORKS

National Institute for Occupational Safety and Health (NIOSH) and Occupational Safety and Health Administration (OSHA) recommend acclimatization, hydration, work–rest cycles, supervision, and, where feasible, physiological monitoring [1], [2]. Professional guidance highlights attention to accuracy, validation, privacy, and acceptance regarding the use of wearable [8]. Bentley Nevada System 1 features plant- wide connectivity and provides analytics (Decision Support) and export interfaces designed for succinct human-health key performance indicators (KPIs) [8], [6].

The Industrial Internet of Things (IIOT) and wearable biosensors have changed the paradigm of occupational health from reactive medical interventions to proactive physiological monitoring. Recent studies highlight the need for monitoring high-risk environments, such as oil and gas fields, due to incidents caused by heat strain and physical fatigue.

I. Commercial Wearable Health Platforms

The efficacy of wearable integration has been demonstrated by current market leaders in clinical-grade monitoring. One such example is Biofourmis, which uses the Biovitals platform. Biovitals [37], which is an AI-powered ecosystem that delivers personalized predictive analytics for patient care. While this platform is very effective in monitoring patients with heart failure and respiratory deterioration, its clinical applications do not integrate with industrial operational data. Kenzen was the first to use wearable heat-stress monitors for industrial workers. Their platform is built to prevent heat illnesses via monitoring real-time core body temperature.

and heart rate. However, it is common for these commercial solutions to operate as “data silos.” This is particularly evident when they are used alongside asset-centric monitoring systems (e.g., Bentley Nevada System 1), which control the equipment that the personnel operate [2].

II. Physiological Strain and Fatigue Analytics

Several academic research papers have demonstrated that there is a high level of correlation between self-reported fatigue and physiological strain. Recent research by Khan et al. (2025) [35], has reinforced the accuracy of wearable sensor-based fatigue classification under various thermal conditions, thereby validating the use of heart rate and skin temperature as reliable physiological measures for assessing worker readiness for work. Furthermore, the National Institute for Occupational Safety and Health (NIOSH) has highlighted that individualized worker safety is more reliable than threshold-based safety protocols, particularly for workers with pre-existing chronic conditions, as they have a higher cumulative risk score.

III. Integration with Industrial Asset Management

While industrial asset health monitoring is a mature field, as evidenced by Bentley Nevada System 1, which provides a connected

asset platform for decision support, the integration of human health "KPIs" with industrial asset health is still in its infancy, with most research focusing on environmental sensors such as WBGT rather than physiological feedback from workers. This paper attempts to address this research gap by proposing a framework that views worker health indicators as critical assets, thereby providing a unified safety platform that links human physiological stability with industrial asset efficiency.

Recent academic contributions have also been made in the realm of the intersection of Ergonomics and Automation. In a Master's thesis, Doe [4] points out the importance of incorporating human biometrics in Industrial Control Systems (ICS). This, in turn, reduces downtime in operations, as it is able to forecast worker exhaustion prior to error occurrence. Another research done in the Oil and Gas industry by Smith [5] points out the lack of conventional safety measures in drilling operations without real-time human physiological feedback, promoting the "Connected Worker" concept.

In the commercial world, both Biofourmis [1] and Kenzen [2] Have already established robust frameworks for health monitoring, but they do not have a direct synergy with machine-level diagnostic tools like Bentley Nevada System 1 [6]. This paper bridges the gap, as identified in recent fatigue classification research [3], by directly linking the worker's physiological state with the operation of the asset."

III. STUDY DESIGN AND STATISTICAL ANALYSIS

A. Study design

This research study investigates the feasibility and acceptability of a biomedical wearable-based predictive health monitoring system integrated with industrial asset monitoring platforms for deployment in oil field environments. The research focuses on assessing whether real-time physiological monitoring combined with rule-based predictive analytics can enhance early detection of occupational heat strain and cardiorespiratory stress among oil field workers. The proposed system was trialed in a simulated operational environment involving workers from the Mellitah Oil & Gas Company at three locations of oil field facilities. This study is not intended to provide any clinical diagnosis; instead, it deals with the engineering feasibility, usability of the system, worker acceptance, and early risk indication capability of the proposed solution under harsh industrial conditions.

The number of participants included in this pilot study was a total of 99 participants ($n = 99$). The number of participants was chosen to enable a preliminary statistical evaluation regarding usability, worker acceptance, and the feasibility of integrating physiological monitoring.

B. Research Objectives and Hypotheses

The objectives of the study were guided by the following:

- Assessment of the prevalence of symptoms of heat stress and fatigue among oil field workers.
- The objective is to assess worker acceptance of wearable-based health monitoring systems.

- The performance, as perceived, of the integration of biomedical health indicators with condition monitoring systems of a more conventional mechanical origin, such as Bentley Nevada System 1.
- To investigate the relationship between chosen physiological measures and subjective ratings of fatigue and symptoms of heat stress.
- Based on these objectives, the following hypotheses were formulated:

H1). The perceived level of fatigue is related to the probability of developing symptoms of heat stress in oil field workers.

H2). Workers with chronic health conditions show higher scores of cumulative physiological risk compared with workers without chronic conditions.

H3). Workers develop a positive attitude towards integrating a wearable biomedical monitoring system with existing industrial safety.

C. Study Population and Sample Size Justification

The sampling for this study included a total of 99 employees from different job categories at Mellitah Oil & Gas Company in three operational fields. The sample size is selected based on the recommendation for pilot and feasibility studies in biomedical and occupational health engineering, with sample sizes of 99 participants being recommended for system feasibility, usability, and preliminary performance assessment prior to large-scale deployment. The study employed a pilot sample suitable for feasibility assessment and system validation, considering that this sample size is appropriate for exploratory statistical analysis and hypothesis testing at the pilot level without claims of generalization on the population level.

D. Data Collection Instruments the two primary instruments used to collect data were: Structured Questionnaire:

A validated structured questionnaire was used to capture demographic characteristics, health experience (heat stress.

Real-time monitoring of heart rate, SpO₂, skin temperature, blood pressure, and glucose levels was simulated using wearable sensors. These signals were fed into a MATLAB-based analytics engine that computes cumulative risk scores and issues alerts if a predefined threshold is exceeded.

E. Statistical Analysis

Descriptive statistics were used to summarize demographic variables, health experience, and levels of acceptance. For these categorical variables, frequencies and percent distribution were reported, while for continuous variables, means and standard deviations were used where applicable.

The following statistical tests have been conducted to check the relationship between the key variables:

The chi-square test was used to test the association between the reported levels of fatigue and symptoms of heat stress (H1). The independent samples t-test was used to compare cumulative physiological risk scores between workers with and without chronic diseases (H2). A one-sample t-test was used to test whether mean acceptance scores for wearable monitoring and system integration were significantly higher than the neutral midpoint of the Likert scale H3. All statistical analyses were performed using IBM SPSS Statistics 24, and the level of significance was set at $p < 0.05$ for all analyses.

F. Ethical and Data Governance Considerations

The study conformed to ethical principles for occupational health research. Participation was voluntary, and all data collected had been

anonymized in advance of analysis. No personal medical data with identifiers was stored in the Monitoring system. Access to data was restricted by using role-based controls, and the collected data were used solely for research and system evaluation purposes.

IV. METHODS

A. System Architecture

Wearable devices are assumed to capture physiological indicators for the purpose of system prototyping and interface testing. Peripheral Capillary Oxygen Saturation (SpO₂) levels, skin temperature, blood pressure, and glucose levels. There is a local analytics layer that filters these signals, applies risk rules for thermal burden and chronic disease flags, and maintains a weekly estimator for field-level absence planning. Summary analytics are pushed to dashboards for viewing.

Wearable Sensing and Data Acquisition Layer. Indeed, in a practical deployment, the simulated physiological signals provided by MATLAB could be replaced by approved signals. Symptoms, fatigue, access to medical services), and attitudes towards wearable health monitoring systems. Attitudinal items' responses were measured using a five-point Likert scale (1–5).

Fig. 1. Health-monitoring architecture: sensing → analytics → Data & Integration Flow



alerts/KPIs.

B. Physiological Monitoring System

wearable biomedical devices that feature continuous measurement of vital parameters pertaining to heart rate, peripheral oxygen saturation (SpO₂), skin temperature, and activity-related strain. Medical-grade wearable systems like

Empatica E4 and Biofourmis Biovitals have already shown their performance in physiological sensing that was clinically validated for remote health monitoring [15], [16].

These devices most often communicate over Bluetooth Low Energy to a proximate gateway, such as a ruggedized smartphone or industrial edge computer carried by the worker or installed in field vehicles. The gateway device aggregates sensor streams and securely transmits them to a central analytics server over cellular or satellite communication networks.

In the proposed architecture, this incoming data stream would feed directly into the analytics engine currently simulated in MATLAB. Preprocessing of the signal, artifact filtering, and feature extraction would precede the computation of individualized physiological risk scores. This is a layered structure that ensures the biomedical sensing subsystem remains modular; device upgrades or replacement can be performed without changing the higher-level predictive or industrial integration layers [6], [8].

Together, these layers—wearable sensing, biomedical analytics, and industrial platform integration—form a closed-loop decision-support ecosystem in which physiological data enhances situational awareness in high-risk industrial environments.

C. MATLAB Implementation (2014-Compatible Graphical User Interface (GUI))

The graphical user interface (1500x800) displays live signals and a weekly trend with a table of employees' Identification Numbers (IDs), fields, and chronic disease markers. Two 25-second timers update values, calculate risk scores, and record critical alerts (score > 5). Upon interruption, a weekly predictor classifies cumulative risks and

estimates expected field-level absences. Listing 1 outlines in MATLAB the basic predictive logic. This function evaluates the cumulative health risks based on vital signs.

Signs (HR, SpO₂, BP, Temp, and Glucose) of all employees under health monitoring, the presence of chronic illness and field location, and calculates the forecasted absenteeism by operational field. Listing 1. Core MATLAB logic for weekly predictive risk and absence estimation.

```
%% Weekly Prediction Logic

function [predicted_absences, absenceRates] =
weeklyPredictionLogic(h) predicted_absences = {};

    cumulative_risk = zeros(h.nEmployees, 1);

    for ii = 1:h.nEmployees

        score = 0;

        if size(h.dataHistory.HR, 2) > 0

            hr = h.dataHistory.HR(ii, end); spo2 = h.dataHistory.SpO2(ii, end);
            temp = h.dataHistory.Temp(ii, end); bp = h.dataHistory.BP(ii,
end);

            glucose = h.dataHistory.Glucose(ii, end);

            if hr > 100 || hr < 60 score = score + 2; end

            if bp > 140 || bp < 90 score = score + 2;

            end

            if temp > 38 || temp < 36 score = score + 1;

            end

            if spo2 < 92

                score = score + 3;

                end

            if glucose > 180 || glucose < 70 score = score + 2;

            end

        end

    end
```

```

        if ~strcmp(h.chronicDiseases{ii}, 'None') score = score + 2;
    end

    cumulative_risk(ii) = score; end

    highRiskEmployees = find(cumulative_risk > 5);

    [~, sortedIdx] = sort(cumulative_risk(highRiskEmployees),
'descend'); num_to_predict = min(3, length(highRiskEmployees));

    for i = 1:num_to_predict

        idx = highRiskEmployees(sortedIdx(i)); employee_info.id =
h.employeeIDs(idx); employee_info.field = h.employeeFields{idx};
predicted_absences{end+1} = employee_info;

    end

    fields = unique(h.employeeFields); absenceRates =
zeros(length(fields),
1);

    for i = 1:length(fields) field = fields{i};

        count = 0;

        for j = 1:length(predicted_absences)

            if strcmp(predicted_absences{j}.field, field) count = count + 1;

        end

    end

    total_in_field = sum(strcmp(h.employeeFields, field));

    if total_in_field > 0

        absenceRates(i) = (count / total_in_field) * 100;

    else

        absenceRates(i) = 0; end

end

end

```

Graphical User Interface and Simulation Logic The predictive health monitoring application was developed in MATLAB-compatible 2014, with a custom-designed GUI intended to simulate real-time occupational physiological monitoring. The GUI is a proof-of-concept

dashboard intended to illustrate the way in which biomedical data could be visualized, analyzed, and operationally interpreted in an industrial environment.

It has three major visual components: an employee monitoring table, a real-time physiological signal visualization panel, and a weekly predictive analytics panel. The employee table displays individual identifiers, assigned operational field, simulated vital signs of heart rate, SpO₂, temperature, blood pressure, and glucose, chronic condition status, and system-generated alert notes.

In the timed data-generation routine, wearable sensor inputs are simulated at fixed intervals, each 25 seconds, representing continuous physiological monitoring. These values are stored in a structured data history array and used for real-time visualization and cumulative risk scoring. This live signal panel plots dynamically the evolution of physiological parameters, providing a visual analogy with streaming biosensor data in real deployments.

A rule-based risk scoring algorithm processes the latest physiological values and assigns weighted risk points based on established occupational health thresholds for tachycardia, hypoxia, hyperthermia, and other clinically relevant indicators, as supported by occupational heat stress and wearable.

D. Integration with Bentley Nevada System 1

We propose three paths:

- 1) Object Linking and Embedding for Process Control (OPC)-based tags for summarized Key Performance Indicators (KPIs).
- 2) Replication to a historian/lake for Decision Support.

Dashboards.

- 3) Alarm bridging so CRITICAL events appear beside asset alarms with metadata (IDs, field, diagnosis) [8], [6].

The main contribution of this work is the conceptual integration of worker physiological health indicators into an established industrial asset monitoring ecosystem; in this context, Bentley Nevada System 1 provides machinery condition monitoring and predictive maintenance for rotating equipment. Proposed here is an extended paradigm that introduces human physiological KPIs alongside mechanical asset metrics.

Integration can be provided by using standard industrial communication protocols such as OPC (OLE for Process Control) or by historian database replication. Within this architecture, the biomedical analytics server exports summarized health risk indicators (cumulative risk score, alert status, workforce strain index) as structured tags compatible with industrial dashboards. These tags are then visualized in System 1 alongside equipment vibration, temperature, and operational load data.

This integrated visualization allows the supervisor to contextualize the operational risk in a holistic sense: both the condition of machinery and human physiological readiness. For instance, if high ambient temperatures are linked to rising worker heat-strain indications, this may provide a pre-emptive adjustment in workload or additional rest cycles. The integration approach follows recent thinking on the connected worker approach to safety and the interlinkage between human- centered monitoring and industrial digital twins [8], [14].

E. Deployment & Governance

The simulation involved 99 employees from Mellitah Oil & Gas Company and covered three operational areas. All employees were provided with wearable devices to test their performance by recording and comparing physiological data. The selected sample size ($n = 99$) aligns with the recommendations of pilot studies in biomedical engineering and occupational engineering. A sample size of 99

participants in the Occupational Health Monitoring and Safety Systems Enhancement Survey for Mellitah Oil & Gas

The company's oilfield workers are considered sufficient to evaluate feasibility and operational readiness and test its feasibility [Van Tegelingen and Hondli, 2001]. This group was chosen to achieve a balanced mix of different job categories, as well as varying levels of environmental exposure and conditions at different work sites. The pilot design and implementation phase included validating the season and the limits associated with the reference measurements, defining key performance indicators (KPIs), and creating a dashboard. Privacy principles were also incorporated into the design (data minimization, role-based access, encryption, and retention limits). This program is considered a simulation to train supervisors and workers on how to use the device, record alerts, and prepare reports to ensure the system is deployed safely and effectively in the future after approval by company management.

F. Data Collection and Quality Assurance

- The data collection for this study aimed at system functionality, usability, and readiness rather than healthcare-related outcomes. There are two sources for data collection used for this study. These are:
 - 1) Data obtained using survey responses by participating employees, and
 - 2) Simulated physiological data used only for testing logic functionality, visualization, and alerts of the system prototype.
- The survey form was designed based on principles long established for occupational health and safety surveys. This ensured that what was being asked was clear, consistent, and appropriate for an industry setting. The questionnaire was also pre- tested before being used.

- The simulated physiological data set was created within known ranges from the literature to confirm that the systems operate properly. These data were not intended for medical-grade applications but for the verification of software functions.

Simple validation procedures have also been undertaken in order to check the quality of the captured survey responses. No personal identifiers are stored in the information gathered, apart from the anonymous identifiers for employees. The project does not require any medical diagnoses for decision- making processes. It did not require any approval for human subjects.

V. RESULTS

A. Socio-demographic Characteristics and Descriptive Analysis of Study Variables.

TABLE I. Gender Distribution of the Study Sample with 95% Confidence Intervals

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Male	89	89.899	82.397	94.420
Female	10	10.101	5.580	17.603

TABLE II. Age Group Categorization and Statistical Prevalence among Participants

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
25–34	36	36.364	27.562	46.184
<25	25	25.253	17.729	34.625
35–44	21	21.212	14.313	30.262

45–54	15	15.152	9.402	23.504
55+	2	2.020	0.556	7.069

TABLE III. Geographic Distribution of Respondents across Mellitah Oil & Gas Operational Fields

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Al-Feel	38	38.384	29.408	48.227
Abu Al-Tifl	31	31.313	23.021	41.002
Mellitah Complex	30	30.303	22.126	39.951

Table IV. Professional Classification And Job Title Distribution Within The Sample

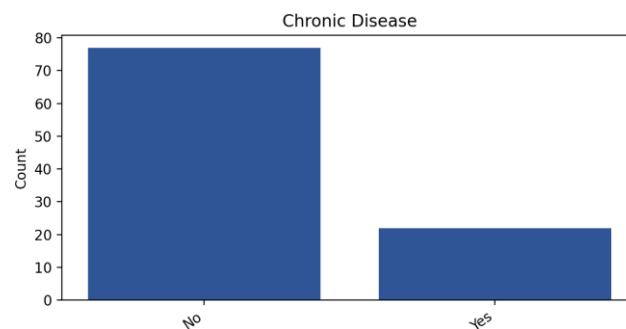
Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Technician	49	49.495	39.851	59.177
Engineer	26	26.263	18.598	35.701
Operator	17	17.172	11.007	25.789
Supervisor	7	7.071	3.467	13.882

TABLE V. Years of Professional Experience and Occupational Tenure of Surveyed Employees

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
<5	34	34.343	25.732	44.125
5–10	32	32.323	23.920	42.047
11–20	21	21.212	14.313	30.262
>20	12	12.121	7.071	20.001

TABLE VI. Self-Reported Prevalence of Chronic Diseases among the Workforce

Category	Count	Percent	CI95_Lower_%	CI95_Upper_%
No	77	77.78	68.64	84.84
Yes	22	22.22	15.16	31.36

**Fig. 2. Distribution of Self-Reported Chronic Diseases among the Workforce (N=99).****TABLE VII. Frequency and Distribution of Occupational Health Emergencies**

Category	Count	Percent (%)	CI95_Lower_%	CI95_Upper_%
No	58	58.586	48.740	67.791
Yes	41	41.414	32.209	51.260

TABLE VIII. Provision of On-site First Aid and Immediate Medical Assistance

Category	Count	Percent	CI95_Lower_%	CI95_Upper_%
No	57	57.58	47.74	66.85

TABLE IX. Proximity and Accessibility of Field Health Facilities to Workstations

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Sometimes	36	36.364	27.562	46.184
Often	25	25.253	17.729	34.625
Rarely	18	18.182	11.822	26.919
Always	11	11.111	6.318	18.809
Never	9	9.091	4.857	16.382

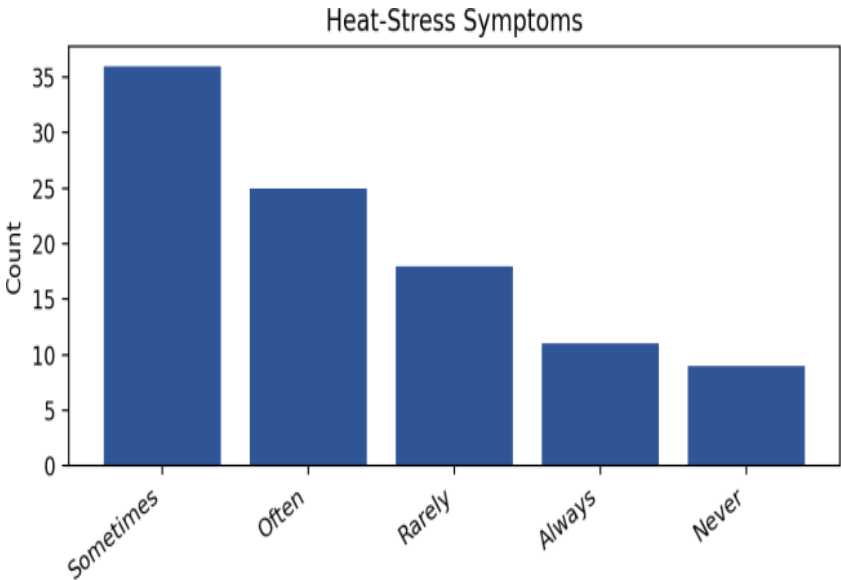


Fig. 3. *Frequency Distribution of Heat-Stress Symptoms among Employees (N=99).*

TABLE X. Employee Evaluation of Health Service Quality in Remote Locations

Category	Count	Percent (%)	CI95_Lower_%	CI95_Upper_%
Moderate	37	37.374	28.483	47.208
Mild	25	25.253	17.729	34.625
Severe	22	22.222	15.158	31.362
Very Severe	8	8.081	4.151	15.142
None	7	7.071	3.467	13.882

TABLE XI. Frequency Analysis of Occupational Heat-Stress Symptoms

Category	Count	Percent	CI95_Lower_%	CI95_Upper_%
No	51	51.52	41.80	61.12
Yes	46	46.46	36.96	56.24
None	2	2.02	0.56	7.07

TABLE XII. Assessment of End-of-Shift Subjective Fatigue Levels

Category	Count	Percent	CI95_Lower_%	CI95_Upper_%
Sometimes	42	42.42	33.15	52.26
Rarely	26	26.26	18.60	35.70
Always	16	16.16	10.20	24.65
Never	15	15.15	9.40	23.50

TABLE XIII. Perceived Quality of Workplace Health Services

Category	Count	Percent	CI95_Lower %	CI95_Upper %
Good	46	46.46	36.96	56.24
Acceptable	35	35.35	26.64	45.16
Poor	10	10.10	5.58	17.60
Excellent	8	8.08	4.15	15.14

TABLE XIV. Primary Barriers and Obstacles to the Adoption of Wearable Sensors

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Heavy/Uncomfortable	36	36.364	27.562	46.184
Awareness/Training	23	23.232	16.009	32.455
Privacy/Data	20	20.202	13.476	29.155
Accuracy	14	14.141	8.614	22.347
none	6	6.06	2,81	12.60

TABLE XV. Major Workplace Safety Challenges Identified by Participants

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Poor training	50	50.505	40.823	60.149
Lack of equipment	19	19.192	12.645	28.041
Non-compliance with procedures	19	19.192	12.645	28.041
Other	11	11.111	6.318	18.809

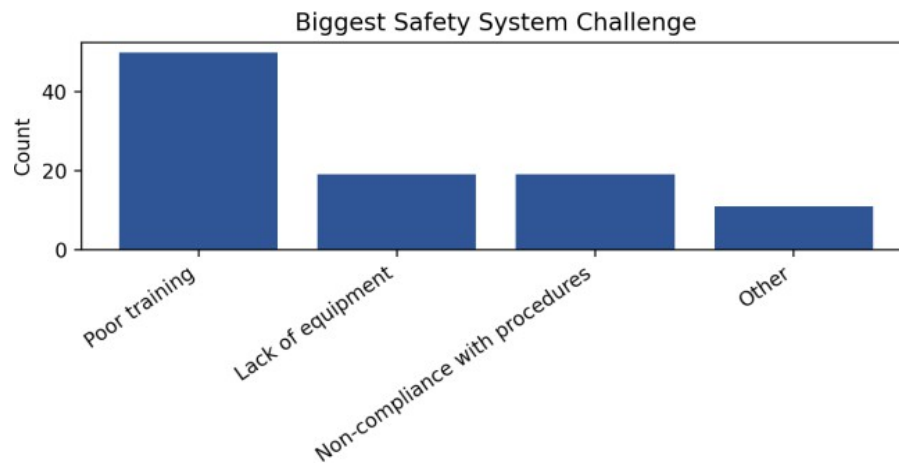


Fig. 4. *Frequency Distribution of Major Workplace Safety Challenges Identified by Participants (N=99).*

TABLE XVI. Workforce Support for Proactive Health Forecasting and Monitoring Systems

Category	Count	Percent (%)	CI95_Lower %	CI95_Upper %
Strongly support	62	62.626	52.792	71.517
Support with reservations	29	29.293	21.237	38.896
Do not support	6	6.061	2.807	12.597
Don't know / not interested	2	2.020	0.556	7.069

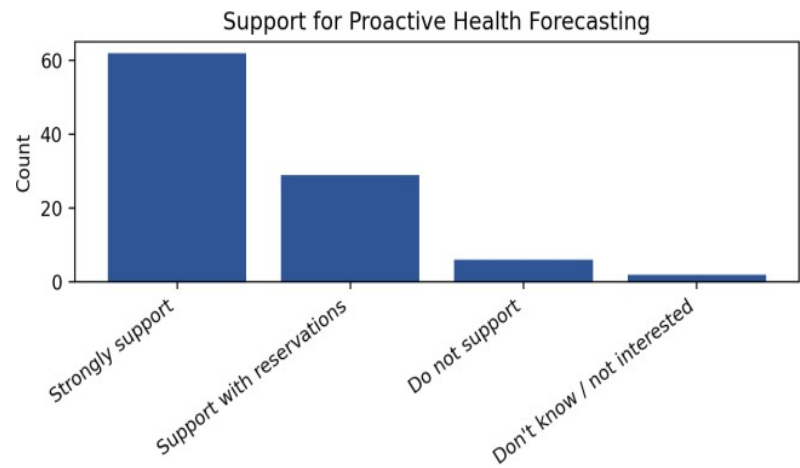


Fig. 5. Employee Support Levels for Proactive Health Forecasting Systems (N=99).

B. Descriptive Analysis of Likert- Scale Responses and Construct Reliability

TABLE XVII. One-Sample t-Test Results: Perceptions of Vital Signs Monitoring and System Integration

Indicator (no code)	Mean	S.D	N	CI 95_ L	CI 95_ U	t(v s3)	p- value	Cohen's d	d_CI_ L	d_CI_ U	Wilcoxon W	Wilcoxon p
Agreement: Monitoring vitals improves safety	3.960	1.151	99	3.730	4.189	8.295	<0.001	0.834	0.580	1.177	387.000	<0.001
Acceptance of wearable sensors	3.804	1.124	97	3.578	4.031	7.046	<0.001	0.715	0.475	1.038	610.000	<0.001
Effective	3.222	1.139	9	2.99	3.44	1.941	0.055	0.195	0.000	0.401	975.00	0.045

ness of tradition al safety systems		9	9	5	9						0	
Integratio n with Bentley Nevada System 1	4.162	0.94 4	9 9	3.97 3	4.35 0	12.23 8	<0.00 1	1.230	0.938	1.618	133.00 0	<0.00 1

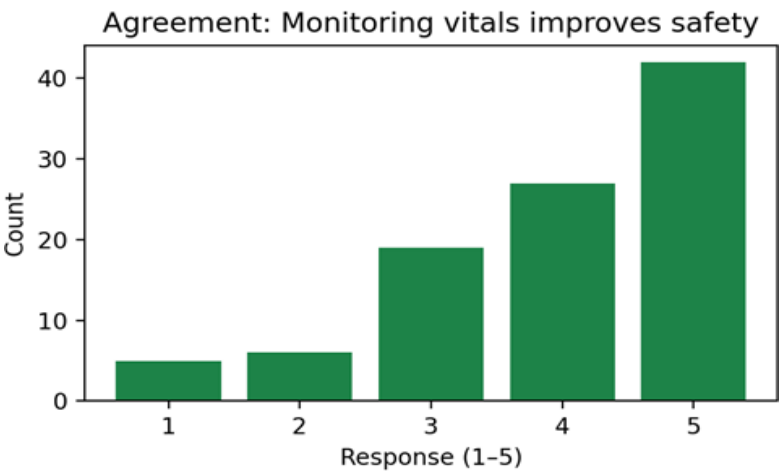


Fig. 6. Mean Agreement Scores for the Impact of Vital Signs Monitoring on Workplace Safety (N=99).

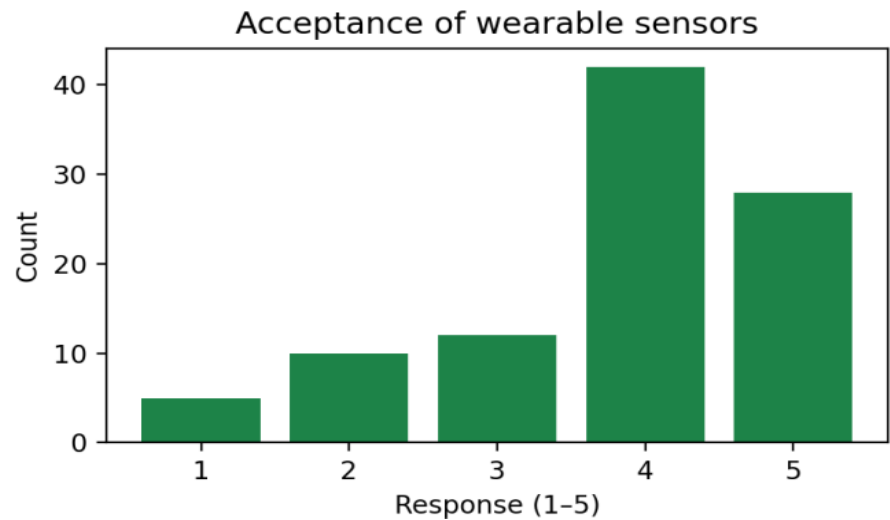


Fig. 7. Acceptance of Wearable Sensors in the Workplace (N=99).



Fig. 8. Perceived Effectiveness of Traditional Health Monitoring Systems (N=99)

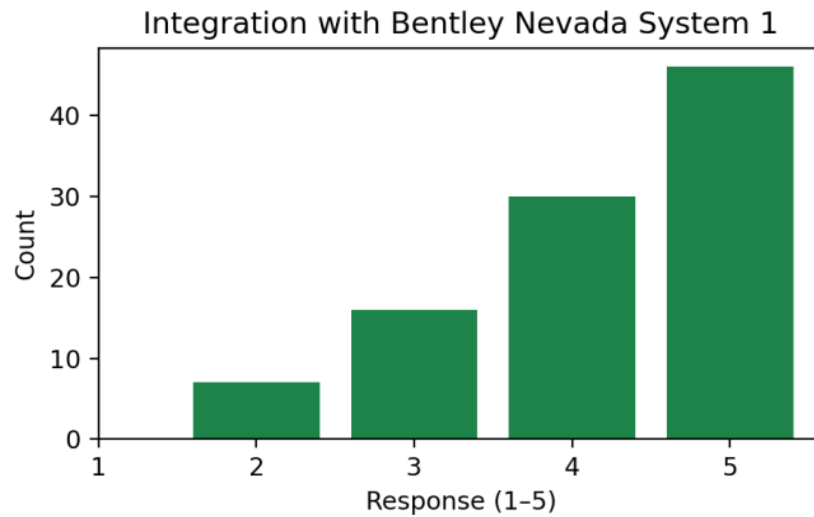


Fig. 9. Perceived Value of Integrating Wearable Data with the Bentley Nevada System 1 (N=99).

C. Hypothesis 1 Testing: Correlation Analysis between Heat-Stress Symptomatology and Fatigue Levels

TABLE XVIII. Statistical Correlation (Spearman's rho and Chi-square) Between Heat-Stress and Fatigue (H1)

Spearman_r	Spearman_p	Chi2	df	Chi_p	Cramers_V
0.381	0.000	30.871	12.000	0.002	0.322

TABLE XIX.Cross-tabulation Analysis: Frequency of Heat-Stress Symptoms vs. Fatigue Severity

Heat_Stress Symptoms	Mild	Moderate	Severe	Very Severe
Never	3	2	1	0
Rarely	11	3	2	2
Sometimes	7	21	5	1
Often	3	7	11	3
Always	1	4	3	2

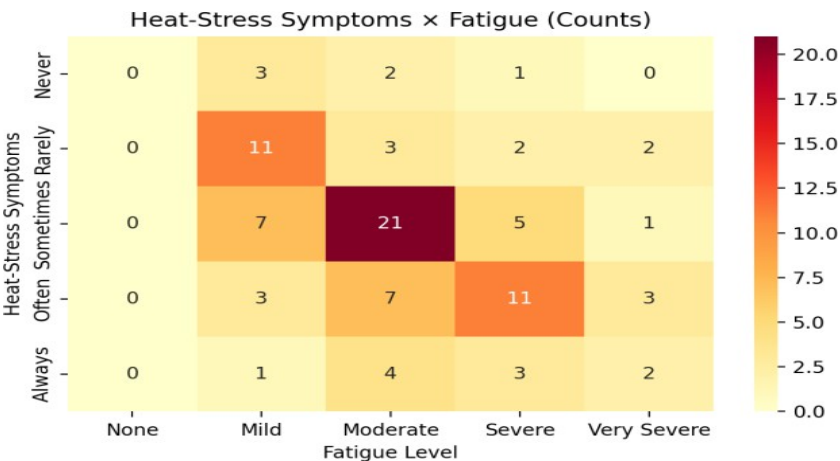


Fig. 10. Heat map Representation of the Association between Heat-Stress Symptoms and Fatigue Levels.

D. Hypothesis 2 Testing: Comparative Analysis of Group Differences (ANOVA/T-test Results)

TABLE XX.Mann–Whitney U Test: Comparative Analysis of Fatigue and Heat-Stress by Chronic Disease Status (H2)

Outcome	U	p-value	n_chronic	n_non_chronic
Fatigue score (ordinal code)	410.500	0.000	22	77
Heat-stress symptoms score (ordinal code)	451.500	0.001	22	77

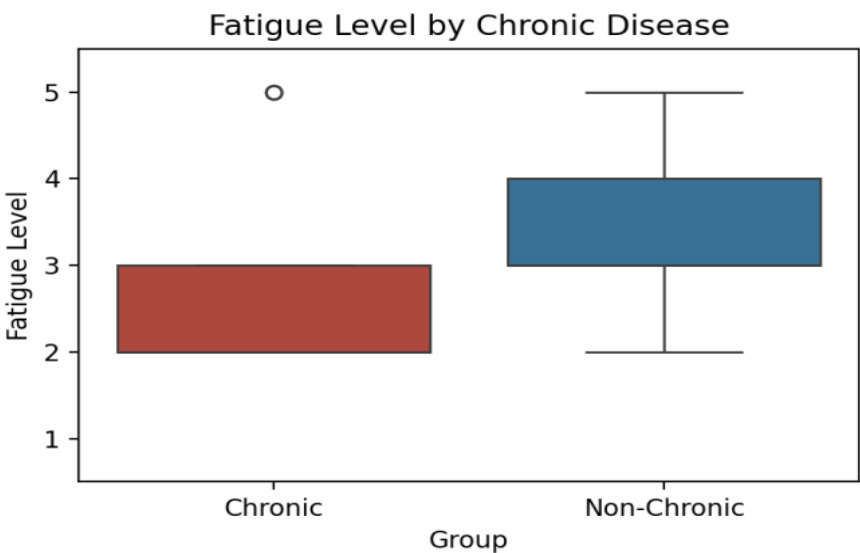


Fig. 11. Comparison of Fatigue Levels between Chronic and Non-Chronic Disease Groups (N=99).

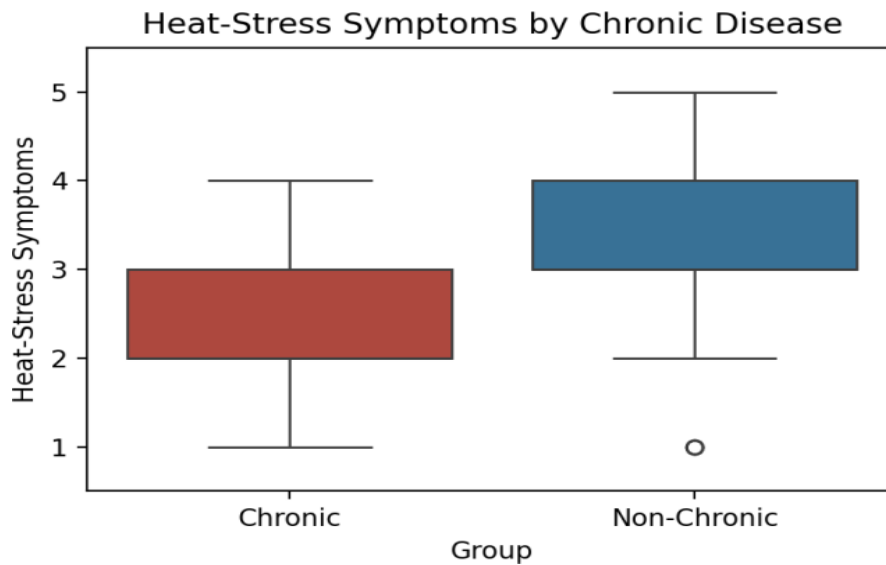


Fig. 12. Distribution of Heat –Stress Symptoms Scores by Chronic Disease Status (N=99).

E. Application Graphical User Interface (Screens) Selected GUI screens: live signals, alerts, weekly predictive trend, and emergency cases view.

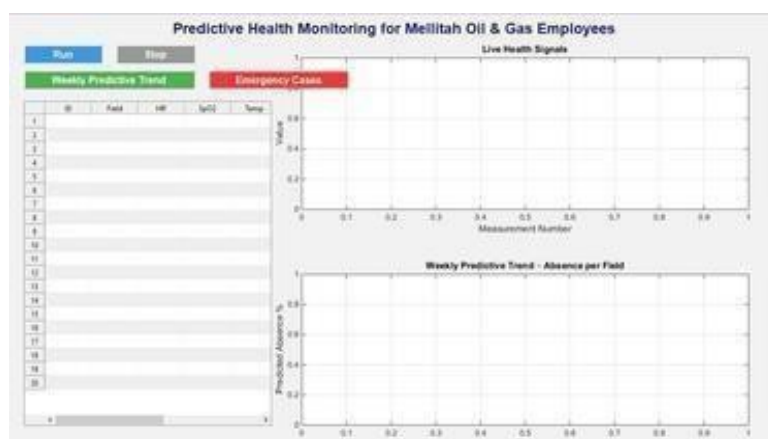




Fig. 15. Graphical user interface (GUI) window displaying logged emergency cases and critical diagnoses generated by the predictive monitoring system.

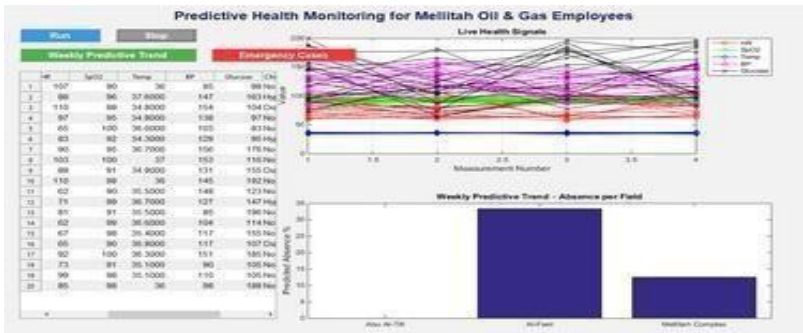


Fig. 16. Real-time visualization of live physiological signals and weekly predictive absence trends in the health-monitoring system.

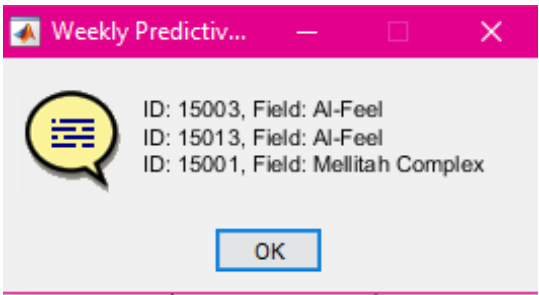


Fig. 17. Notification window displaying weekly predictive alerts for high- risk employees across Mellitah Oil & Gas fields.

VI. DISCUSSION

This study shows that adding wearable health monitors to industrial safety systems greatly improves the early detection of health risks in tough environments. A strong link was found between fatigue and heat stress symptoms (Spearman's $\rho = 0.381$, $p < 0.001$), indicating that fatigue is a clear sign of cumulative physiological strain instead of just a feeling. The much higher fatigue and heat stress scores among workers with chronic conditions ($p < 0.001$) point to the need for personalized monitoring. By setting individual physiological baselines and adjustable risk levels, biomedical systems can go beyond fixed, general exposure limits to offer tailored protection for at-risk workers. The high acceptance of this monitoring among workers shows that human-centered monitoring is both technically and socially workable in the oil and gas industry. Incorporating these physiological indicators into existing platforms, like Bentley Nevada System 1, creates a comprehensive "human-asset" safety strategy. This setup allows for real-time decision-making during high-risk times, like maintenance shutdowns or extreme heat events, effectively moving industrial safety from a reactive approach to a proactive, data-driven prevention method.

A. Limitations and Future Work

While these results are encouraging, there are several limitations to consider. This pilot study involved 99 participants and used simulated physiological data, which, although it validated the analytical framework, needs further checks with medical-grade wearables (e.g., Empatica E4) in real field conditions. Additionally, the cross-sectional design prevents clear.

Summary about causality. Future versions of the model should include real-time environmental data, such as Wet Bulb Globe Temperature (WBGT), and shift from self-reported data to continuous biometric monitoring to reduce recall bias and improve predictive accuracy. In

the end, this work lays the groundwork for large-scale clinical validation in industrial settings.

VII. CONCLUSION

This research confirms the potential for incorporating tools of Biomedical engineering in industrial monitoring Environments for decision support in occupational safety. The result confirms technical validity and worker acceptance, as well as a need for further validation. Proactive prediction—using certified wearable devices, Matrix Laboratory (MATLAB) analytics, and Bentley Nevada System 1 visualizations—provides a practical pathway to scaling up worker safety programs in remote operations characterized by high temperatures, harsh conditions, and a lack of nearby health facilities. This work demonstrates how biomedical engineering principles can be practically embedded within existing industrial monitoring infrastructures to enhance worker-centered safety without disrupting operational workflows.

VIII. RECOMMENDATIONS

- Collaboration and Design with Workers: Testing various sensors and tape materials in short, purpose-built trials.
- Reducing Monitoring Issues: Pre-pairing devices, automating calibration checks, and providing backup charging units at the start of each shift.
- Adjusting Work Limits: Modifying alerts based on local environmental conditions (such as Wet Bulb Globe Temperature (WBGT) and heat stress) and the type of work performed.
- Protecting Privacy: Minimizing data and promoting role-based transparency, with limited data required for safe action, reinforces a due diligence approach.

- Impact Assessment: Analyzing near misses, initial emergencies, and unplanned downtime to assess impact and inform expansion plans.
- Expansion: In the future, easily liftable/localized sensors will be integrated, and the possibility of humidity monitoring for the next phase of work will be explored.
- Collaborating with Italian partner Eni to evaluate the latest advancements in occupational safety.
- Develop and expand the monitoring and forecasting program for Mellitah Oil and Gas Company employees, which was presented in this research paper, to be applied by the company's management to all employees in its fields.

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**Functional Electrical Stimulation (FES)
in Post-Stroke Rehabilitation:
Technological Advancements and
Engineering Applications**

Functional Electrical Stimulation (FES) in Post-Stroke Rehabilitation: Technological Advancements and Engineering Applications

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Abstract

Stroke remains a leading cause of motor disability globally, with approximately 85% of survivors experiencing significant limb weakness or paralysis.

Functional Electrical Stimulation (FES) is an established neurorehabilitation technique that aims to restore functional movement by applying electrical pulses to motor nerves. The role of FES extends beyond merely inducing muscle contraction; it significantly contributes to enhancing Neuroplasticity by activating central neural and sensory pathways.

This paper reviews the physiological principles and neural mechanisms of FES, with a particular focus on the recent technological and engineering advancements in FES systems. Advanced control systems, such as FES-BCI and FES-EMG, represent a major leap forward in improving clinical outcomes for post-stroke patients.

Keywords—Functional Electrical Stimulation, Stroke, Neurorehabilitation, Biomedical Engineering, Brain-Computer Interface (BCI), Electromyography (EMG).

I. INTRODUCTION

Stroke is defined as the sudden onset of a neurological deficit resulting from a partial or complete interruption of blood supply to a specific region of the brain [1]. It is the second leading cause of death and the third leading cause of combined death and disability worldwide [2]. Stroke often results in weakness or paralysis (Hemiparesis) of the limbs, severely impacting patient independence and quality of life [3].

In the context of rehabilitation, Functional Electrical Stimulation (FES) has emerged as a potent tool for functional movement restoration. FES operates on the principle of applying electrical

pulses via surface electrodes to stimulate motor nerves, thereby eliciting a functional contraction in the targeted muscles [4].

This technology holds particular significance in biomedical engineering conferences due to its continuous evolution, which involves the design of more precise control devices, the development of optimized stimulation protocols, and its integration with advanced technologies like Brain-Computer Interfaces (BCI) [5].

II. PHYSIOLOGICAL MECHANISMS AND NEURAL EFFECTS OF FES

1. FES Mechanism on Muscles and Nerves

FES generates an Action Potential in motor nerves, which subsequently triggers muscle contraction. However, the recruitment of muscle fibers by FES differs from voluntary contraction; FES primarily targets superficial muscle fibers with a lower electrical threshold (Fast-twitch fibers), which explains the strong contraction and rapid onset of muscle fatigue [6].

Beyond direct motor stimulation, FES contributes to:

Neuroplasticity: Electrical pulses stimulate sensory fibers, sending signals to the spinal cord and brain, which promotes Neural Reorganization in the motor cortex [4].

Muscle Conditioning: FES helps stimulate protein synthesis pathways within the muscle, increasing muscle mass and reducing atrophy [7].

2. FES Applications in Post-Stroke Phases

FES can be applied in both the subacute and chronic phases following a stroke [8]. Studies have consistently shown that applying FES in the early stages of rehabilitation leads to better clinical outcomes compared to delayed initiation [9]. Optimal results are typically observed when FES is combined with the patient's voluntary effort or neural signals, which significantly enhances motor learning [10].

III. ENGINEERING ADVANCEMENTS IN FES SYSTEMS

Modern FES devices consist of a pulse generation unit, control and processing unit, stimulation electrodes, and power supply. Pulse generators typically deliver biphasic pulses with frequencies between 20–50 Hz and pulse widths ranging from 50–400 μ s. Microcontrollers implement stimulation algorithms and integrate feedback from sensors such as inertial measurement units (IMUs).

A.FES Device Design and Engineering Components

Modern FES devices consist of several key engineering components [21]:

Pulse Generation Unit: Responsible for generating electrical pulses (typically biphasic and asymmetrical) at a high voltage [22]. This unit must allow for precise control over stimulation parameters:

Frequency: Typically ranges between 20–50 Hz.

Pulse Width: Ranges between 50–400 microseconds.

Amplitude: Controlled to adjust the force of muscle contraction.

- 1. Control and Processing Unit:** The "brain" of the device, often utilizing microcontrollers to execute complex stimulation protocols and process feedback signals from sensors.
- 2. Electrodes:** Used to deliver the current to the skin. They must have low impedance and be suitable for minimizing skin discomfort.

TABLE I: ELECTRODE ENGINEERING: SURFACE VS. IMPLANTED

<i>Feature</i>	<i>Surface</i>	<i>Implanted</i>
----------------	----------------	------------------

	<i>Electrodes</i>	<i>Electrodes</i>
Selectivity	Low (Stimulates adjacent muscles)	High (Target specific motor points)
Invasiveness	Non-invasive	Requires surgery
Impedance	High (Skin barrier)	Low (Direct nerve contact)
Maintenance	Frequent replacement/repositioning	Stable long-term positioning

3. Power Unit: Usually rechargeable batteries, with devices designed to be compact and portable for daily use [23].

B. Movement Intention-Driven FES (EMG-Triggered FES)

This approach integrates the FES device with an Electromyography (EMG) sensor. Electrical stimulation is only initiated when the device records electrical activity (EMG) from the targeted muscle, linking the patient's motor intention with the actual movement [12].

Engineering Aspect: This system requires a precise control circuit for processing the EMG signal (amplification, filtering, and thresholding) to ensure stimulation synchronizes with the voluntary neural command, thereby promoting motor learning and reducing overstimulation [12].

TABLE II: EMG-TRIGGERED FES VS BCI-FES

Feature	EMG-Trig gered FES	BCI-FES	Engineering Implication
Signal source	Residual EMG muscle	EEG brain signals	Different sensing hardware required
Latency	Low	Moderate - High	EEG processing increases delay
Accuracy	High when voluntary activity exists	Moderate	Signal classification challenges
Setup complexity	Simple	Complex	Requires EEG electrodes and calibration

C. Brain-Computer Interface and FES (BCI-FES)

The BCI-FES system represents the pinnacle of technical development in this field, utilizing brain signals (EEG) to directly control FES activation [14].

Engineering Aspect: The system comprises three main modules [15]:

1.1 Sensing Unit: EEG sensors capture neural signals.

Processing and Control Unit: Complex algorithms process EEG signals, extract features, and classify movement intention (e.g., using AI algorithms like CSP and SVM) [16].

AI is increasingly used to classify patterns such as Visual Evoked Potential (VEP) or Motor Imagery [24] [25].

1. Stimulation Unit: The FES device applies pulses based on the controller's output.

Outcomes: BCI-FES systems have demonstrated a moderate effect in restoring upper limb function and enhancing neuroplasticity through the simultaneous stimulation of sensory and motor systems [14] [17].

IV. ENGINEERING CHALLENGES AND ADVANCED CONTROL STRATEGIES

Advanced FES systems necessitate sophisticated control strategies to ensure optimal performance:

1. Muscle Fatigue and Torque Control Challenge

The recruitment of fast-twitch fibers by FES leads to rapid muscle fatigue.

Engineering Solution: Strategies have been proposed for the simultaneous modulation of stimulation intensity and frequency to improve joint controllability and muscle endurance [18]. Mathematical models (such as the "pedal hill" model) have also been developed to determine the optimal stimulation mode for maximum torque efficiency [19].

Torque Control Model

A simplified model used in FES control for muscle torque generation is:

$$\tau = K.A.f(1 - e^{\frac{t}{\tau(fatigue)}})$$

Where:

τ	generated joint torque
k	Muscle-specific gain constant
a	stimulation amplitude

f	stimulation frequency
t	stimulation time
τ_{fatigue}	Fatigue time constant describing muscle performance decay.

2. Closed-Loop Control Systems

To achieve smooth and accurate movements, FES systems must operate in a Closed-Loop fashion, where feedback from sensors is used to adjust stimulation parameters in real-time [26].

Sensors: Advanced sensors like Inertial Measurement Units (IMUs) and pressure sensors are used to provide accurate feedback on limb position, velocity, and contraction force [20].

Control Algorithms: Adaptive Control or Model Predictive Control algorithms are applied to adjust stimulation intensity, compensating for changes in muscle response and fatigue [27].

V. CLINICAL EFFICACY OF FES IN POST-STROKE REHABILITATION

A. Numerous systematic reviews and meta-analyses have confirmed the efficacy of FES in improving clinical outcomes [28]:

TABLE III: FES EFFICACY & CLINICAL GOAL

<i>Clinical Goal</i>	<i>Observed Outcome</i>	<i>Evidence Summary</i>
Upper limb recovery	Improved Fugl-Meyer scores	Observed in randomized rehabilitation trials
Shoulder	Reduced joint	Early FES intervention

subluxation prevention	displacement	beneficial
Gait improvement (foot drop)	Improved ankle ROM and walking speed	Reported in multiple clinical trials
Neuroplasticity enhancement	Increased cortical activation	Particularly with BCI-FES systems

B. Patient Selection Criteria

Successful FES intervention requires specific baseline criteria:

- 1. EMG-Triggered:** Patients must exhibit a minimum residual EMG amplitude (typically $>5\text{mV}$) to trigger the stimulator.
- 2. Cognitive Status:** Patients must be able to follow multi-step instructions, especially for BCI-FES.
- 3. Safety:** Absence of cardiac pacemakers or severe skin lesions at electrode sites

VI. CONCLUSION AND FUTURE OUTLOOK

Functional Electrical Stimulation (FES) represents a vital technological solution in the rehabilitation of stroke patients. The integration of FES with advanced biomedical engineering technologies, such as BCI and EMG-triggered FES systems, has led to a paradigm shift in treatment efficacy. These sophisticated systems, relying on complex signal processing algorithms and precise control strategies, not only work to restore movement but also enhance neuroplasticity, underscoring the role of biomedical engineering as a

fundamental pillar in developing innovative solutions to improve the quality of life for stroke survivors.

1. **Limitations:** Current BCI-FES systems require extensive user training (15–20 sessions) to achieve reliable control and may not be suitable for patients with severe cognitive impairment.
2. **Future Outlook:** Development of wearable, soft-robotic integrated FES devices is expected to dominate the field accuracy of movement intention classification and personalize stimulation protocols for individual patients.

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**Interpretable Machine Learning
Framework for Predicting Cisplatin
Response in Lung Cancer Using Gene
Expression Data**

38

Interpretable Machine Learning Framework for Predicting Cisplatin Response in Lung Cancer Using Gene Expression Data

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Abstract

Predicting the response to chemotherapy remains a significant challenge in precision oncology, particularly for commonly used agents such as Cisplatin in lung cancer treatment. The heterogeneity of tumors contributes to considerable variability in treatment

outcomes, which can lead to ineffective therapeutic decisions and unnecessary toxicity.

In this study, an interpretable machine learning framework is developed to predict Cisplatin sensitivity based on gene expression data. Transcriptomic profiles obtained from the Cancer Cell Line Encyclopedia (CCLE) were integrated with pharmacogenomic response data from the Genomics of Drug Sensitivity in Cancer (GDSC). A feature selection approach was employed to identify a compact set of biologically relevant genes associated with drug response. The selected features were subsequently used to train a binary classification model using the Extreme Gradient Boosting (XGBoost) algorithm.

The developed model achieved reliable classification performance, with an accuracy of 0.79 and an ROC-AUC of 0.85 on the test dataset, outperforming several baseline methods. Furthermore, the model demonstrated consistent generalization when evaluated on an independent dataset, indicating its robustness across different pharmacogenomic cohorts.

To enhance model interpretability, SHapley Additive exPlanations (SHAP) were applied to quantify the contribution of individual genes to the prediction outcomes. Among the identified features, SLFN11 emerged as a key biomarker, consistent with previous studies highlighting its role in mediating sensitivity to DNA-damaging agents. In summary, the proposed framework combines predictive performance, interpretability, and cross-dataset validation, while identifying a compact set of genes associated with Cisplatin response. These results highlight the potential of interpretable machine learning approaches for biomarker-driven prediction of chemotherapy response in precision oncology.

Keywords—Cisplatin sensitivity, Lung cancer, Gene expression, Pharmacogenomics, XGBoost, SHAP, Drug response prediction, Precision oncology

I. Introduction

Lung cancer remains one of the leading causes of cancer-related mortality worldwide and continues to pose a significant global health burden [1]. Despite advances in early Cisplatin is one of the most commonly used agents in this class and exerts its therapeutic effect by inducing DNA damage and promoting apoptosis in rapidly proliferating cancer cells [10]. Nevertheless, considerable variability in patient response to Cisplatin has been widely reported, highlighting the need for predictive approaches capable of identifying tumors likely to respond to treatment [5].

Recent advances in high-throughput genomic technologies have enabled large-scale characterization of cancer cell lines and their molecular profiles. Publicly available resources, including the Cancer Cell Line Encyclopedia (CCLE) and the Genomics of Drug Sensitivity in Cancer (GDSC), provide comprehensive datasets linking gene expression profiles with pharmacological responses across numerous cancer cell lines [1], [2].

These datasets have become essential resources for developing computational models aimed at predicting drug sensitivity based on molecular features [2]. In this context, machine learning techniques have been increasingly applied to drug response prediction [5], [6]. These approaches enable the identification of predictive biomarkers and support the development of models capable of estimating drug sensitivity prior to treatment [7].

Such frameworks are particularly relevant in precision oncology, where treatment decisions are guided by molecular characteristics rather than relying solely on traditional clinical factors [3].

More recently, both machine learning and deep learning approaches have been widely utilized to model cancer drug responses using large-scale pharmacogenomic datasets [5], [6]. For example, the DrugCell framework integrates genomic mutation data with drug-related

features through a biologically informed neural network architecture, enabling partially interpretable predictions based on hierarchical biological knowledge [4]

Despite these advances, several methodological challenges remain. Many existing studies rely on complex deep learning models trained on large pharmacogenomic datasets such as GDSC and CTRP [2], [6]. Although these models often achieve strong predictive performance, their complexity limits interpretability and hinders the identification of biologically meaningful biomarkers associated with therapeutic response [5], [7].

In addition, a considerable number of studies focus on multi-drug prediction rather than drug-specific modeling, which is more relevant for precision oncology applications [6]. Furthermore, many approaches rely on high-dimensional feature spaces without identifying compact gene signatures that could be translated into practical clinical biomarkers [5], [7]. Another limitation is the reliance on internal validation, while evaluation on independent datasets remains relatively limited, raising concerns regarding model robustness and generalizability [5], [6].

Another limitation is the reliance on internal validation, while evaluation on independent datasets remains relatively limited, raising concerns regarding model robustness and generalizability [5], [6]. To address these challenges, this study proposes an interpretable machine learning framework for predicting Cisplatin response specifically in lung cancer using gene expression data. Unlike many previous studies that rely on complex deep learning models or multi-drug prediction strategies, our approach focuses on drug-specific modeling and identifies a compact set of biologically relevant genes while maintaining strong predictive performance across independent pharmacogenomic datasets. This framework aims to provide molecular determinants of sensitivity, addressing an open problem in precision oncology [3].

II. MATERIALS AND METHODS

Figure 1 presents the overall workflow of the proposed framework for predicting Cisplatin response. The framework consists of a sequence of steps, including data integration, preprocessing, feature selection, model training, and performance evaluation.

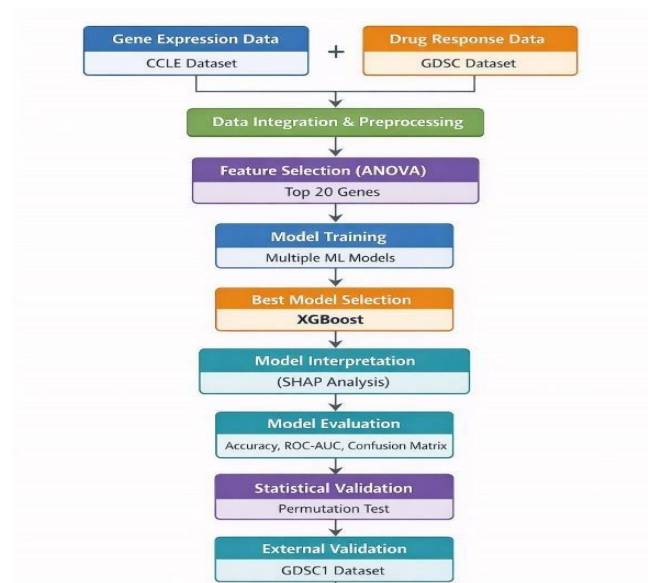


Fig. 1. Workflow of the Proposed Cisplatin Response Prediction Framework

A. Dataset Sources

This study utilizes gene expression data obtained from the Cancer Cell Line Encyclopedia (CCLE) RNA-sequencing dataset, which provides large-scale transcriptomic profiles covering a broad spectrum of cancer cell lines [1]. The dataset initially comprised gene expression measurements for 1,406 cell lines and approximately 53,970 gene features, reflecting genome-wide transcriptional activity.

Drug response data were obtained from the Genomics of Drug

Sensitivity in Cancer (GDSC) pharmacogenomic database [2], which includes experimentally measured responses of cancer cell lines to a wide range of anticancer drugs. In this work, particular attention was given to Cisplatin due to its widespread use in lung cancer treatment.

To construct the final dataset, gene expression profiles from CCLE were integrated with drug response data from GDSC using shared cell line identifiers, ensuring consistency between molecular features and drug response measurements [1], [2].

B. Drug Response Processing

The response to Cisplatin was quantified using the half- maximal inhibitory concentration (IC₅₀), defined as the drug concentration required to reduce cell viability by 50% [2], [21].

To formulate the problem as a binary classification task, IC₅₀ values were categorized into two groups representing Cisplatin-sensitive and Cisplatin-resistant cell lines. Following commonly adopted practices in pharmacogenomic studies, the median IC₅₀ value was used as the threshold for classification [6], [21].

This transformation allows the application of supervised machine learning algorithms to identify molecular patterns associated with variations in drug response [5], [20].

C. Data Integration and Preprocessing

Gene expression data were integrated with Cisplatin response data using shared identifiers between the CCLE and GDSC datasets [1], [2].

After aligning the datasets, filtering was performed to retain only lung cancer samples with complete gene expression and drug response information. This process resulted in a final dataset of 565 samples, which were divided into 452 samples for training and 113 samples for testing.

The original gene expression matrix contained more than 53,000 features, reflecting the high dimensionality characteristic of transcriptomic data [5], [22]. To address this, preprocessing steps were applied to ensure consistency across samples and to prepare the data for machine learning analysis [23].

D. Feature Selection

Gene expression datasets are typically characterized by a large number of features relative to the number of available samples. This imbalance can increase the risk of overfitting and reduce the interpretability of the model [5], [6], [23].

To address this issue, feature selection was performed to identify the most relevant genes associated with drug response [22].

In this context, feature importance scores derived from the XGBoost algorithm were used to rank gene features based on their contribution to model performance [3], [24]. XGBoost constructs an ensemble of gradient-boosted decision trees and estimates the importance of each feature during the learning process. Based on these importance scores, the top 20 most informative genes were selected for model development [6], [22].

E. Machine Learning Model

In the initial stage, several baseline machine learning algorithms were evaluated, including Logistic Regression, Random Forest, and Support Vector Machine (SVM), in order to establish performance benchmarks [5], [20]. Following this comparison, XGBoost was selected as the final predictive model due to its strong performance and its ability to capture nonlinear relationships in high-dimensional data.

In addition, it provides interpretable feature importance measures [3], [24]. Model hyperparameters were carefully configured to achieve

an appropriate balance between model complexity and generalization capability on unseen data [23].

F. Model Evaluation

The performance of the proposed model was assessed using several standard classification metrics, including accuracy, precision, recall, F1-score, and the area under the ROC curve (ROC-AUC) [5]. Accuracy reflects the overall proportion of correctly classified samples, while precision and recall provide deeper insight into the model's ability to correctly identify sensitive and resistant cases.

The F1-score represents a harmonic balance between precision and recall and is particularly useful in scenarios with potential class imbalance. ROC-AUC was further employed to evaluate the model's ability to discriminate between classes across different decision thresholds.

The XGBoost model was configured using the following hyperparameters: learning rate = 0.1, maximum tree depth = 6, and number of estimators = 100. Additional parameters, including subsample and colsample_bytree, were adjusted to reduce overfitting and enhance model robustness.

Furthermore, a confusion matrix was used to provide a detailed evaluation of classification performance by illustrating the distribution of true positives, true negatives, false positives, and false negatives. The ROC curve corresponding to the model performance is presented in the Results section.

G. Model Interpretation

To enhance the interpretability of the proposed model, SHapley Additive exPlanations (SHAP) were employed to analyze the contribution of individual gene features to the model predictions [4]. SHAP is an explainable artificial intelligence approach grounded in

cooperative game theory, which assigns contribution values to each feature based on its impact on the prediction outcome.

This method allows for a detailed examination of how specific gene features influence the prediction of Cisplatin sensitivity or resistance. By quantifying feature contributions, SHAP provides insight into the relative importance of each gene in the decision-making process of the model.

As illustrated in Figure 2, the SHAP analysis offers a clear visualization of feature importance along with the direction of influence for each gene. This facilitates a more intuitive understanding of how variations in gene expression affect model predictions.

Furthermore, the application of SHAP supports the identification of biologically relevant genes that may play a role in determining drug response.

Such insights can contribute to the discovery of potential molecular biomarkers associated with Cisplatin sensitivity, thereby enhancing the clinical relevance of the proposed predictive framework [4], [25].

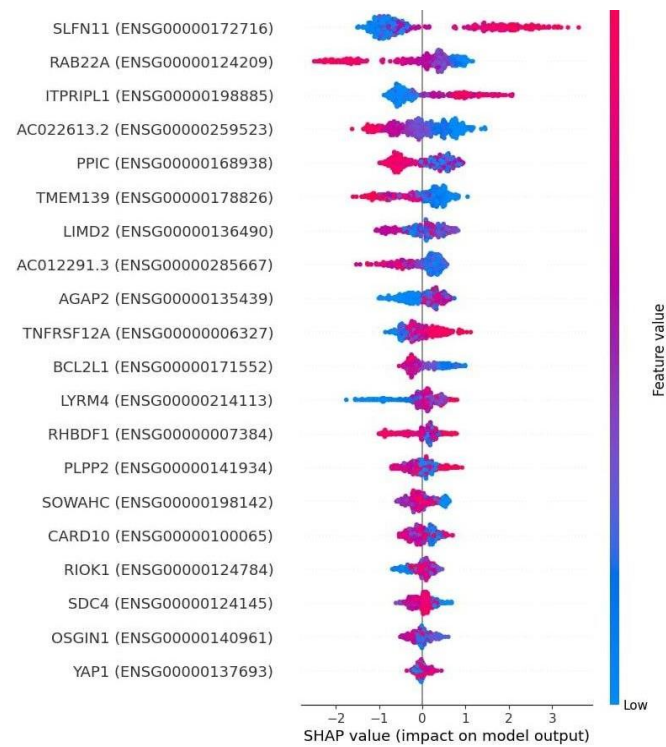


Fig. 2. SHAP Gene Contribution for Cisplatin Sensitivity Prediction

III. RESULTS

A. Predictive Performance of the Proposed Model

The predictive capability of the proposed framework was assessed using gene expression profiles derived from lung cancer cell lines. Model training was performed on the GDSC2 dataset, followed by validation on the independent GDSC1 cohort, both obtained from the Genomics of Drug Sensitivity in Cancer (GDSC) resource [2]. This

setup allows for a more reliable evaluation of the model's ability to generalize across datasets.

To benchmark performance, several baseline classifiers were evaluated, including Logistic Regression, Random Forest, Support Vector Machine (SVM), Gradient Boosting, and K-Nearest Neighbors (KNN). Among these approaches, XGBoost consistently outperformed the other models in terms of both accuracy and discriminative power, which justified its selection as the final predictive model [3].

On the held-out test portion of the GDSC2 dataset, the XGBoost model achieved an accuracy of 0.79 and an ROC- AUC of 0.85. These results indicate a strong ability to distinguish between Cisplatin-sensitive and resistant cell lines. An AUC exceeding 0.80 generally reflects that the model is capturing meaningful biological patterns within the high-dimensional gene expression space rather than relying on dataset-specific noise.

When applied to the independent GDSC1 dataset, the model maintained a comparable level of performance, supporting its robustness and generalization capability across different dataset releases. This is particularly important given the known batch effects and experimental variability between different versions of GDSC [2].The ROC curve corresponding to the XGBoost model is shown in Figure 3.

A detailed comparison of model performance across all evaluated classifiers is provided in Table I the evaluated classifiers exhibit varying performance in terms of accuracy, ROC-AUC, and other evaluation metrics

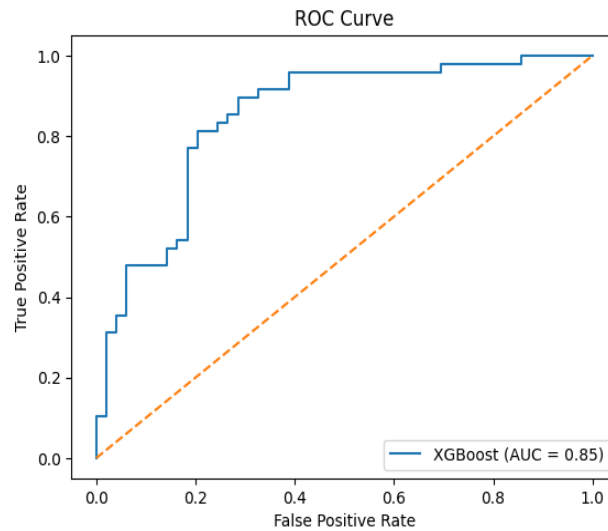


Fig. 3. ROC Curve for Cisplatin Sensitivity Prediction

TABLE I. PERFORMANCE COMPARISON OF EVALUATED CLASSIFIERS

Model	Accuracy	AUC
XGBoost	0.79319	0.84913
Random Forest	0.70103	0.82398
SVM	0.72164	0.82355
Gradient Boosting	0.73195	0.81377
Logistic Regression	0.72164	0.80654
KNN	0.68041	0.75233

These findings are consistent with prior studies demonstrating the effectiveness of XGBoost [3] as well as recent pharmacogenomic prediction frameworks based on machine learning approaches [5], [6].

B. Important Gene Features Identified by the Model

Feature selection reduced the original high-dimensional gene expression space to a compact subset of 20 informative genes. These features were ranked based on their contribution to model performance as estimated by XGBoost feature importance scores.

Among the top-ranked genes, ITPRIPL1, SLFN11, and AC022613.2 exhibited the highest importance values. Notably, SLFN11 also demonstrated the strongest contribution in the SHAP analysis, indicating a consistent influence across both model-specific and model-agnostic interpretability approaches.

The identification of SLFN11 is particularly relevant, as previous studies have demonstrated its role in sensitizing cancer cells to DNA-damaging agents, including platinum-based chemotherapy such as Cisplatin across multiple cancer types [9], [10].

This suggests that the model captures biologically meaningful signals rather than purely statistical associations.

The full ranking of the top 20 genes is illustrated in Figure 4, while their detailed importance values are summarized in Table II

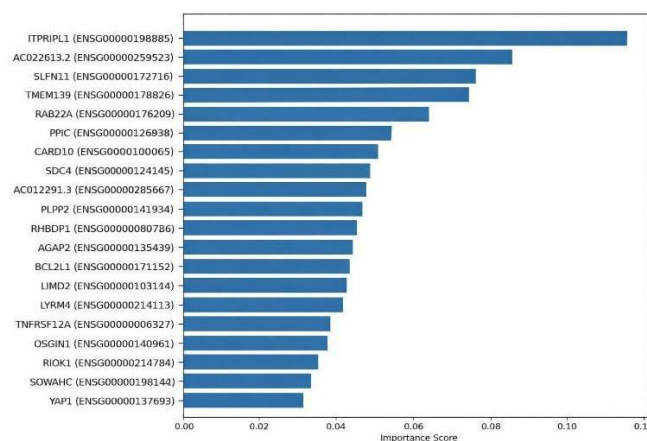


Fig. 4. Top 20 Gene Importance for Cisplatin Sensitivity Prediction

TABLE II. TOP 20 GENES AND THEIR IMPORTANCE SCORES

Gene Symbol	Ensembl ID	Importance Score
ITPRIPL1	ENSG00000198885	0.1148
AC022613.2	ENSG00000259523	0.0830
SLFN11	ENSG00000172716	0.0726
TMEM139	ENSG00000178826	0.0709
RAB22A	ENSG00000124209	0.0617
PPIC	ENSG00000168938	0.0521
CARD10	ENSG00000100065	0.0480
SDC4	ENSG00000124145	0.0454
AC012291.3	ENSG00000285667	0.0446
PLPP2	ENSG00000141934	0.0436
RHBDF1	ENSG00000007384	0.0418
AGAP2	ENSG00000135439	0.0411
BCL2L1	ENSG00000171552	0.0399
LIMD2	ENSG00000136490	0.0395
LYRM4	ENSG00000214113	0.0381
TNFRSF12A	ENSG00000006327	0.0376
OSGIN1	ENSG00000140961	0.0333
RIOK1	ENSG00000124784	0.0331
SOWAHC	ENSG00000198142	0.0304
YAP1	ENSG00000137693	0.0285

Overall, these findings support the hypothesis that a relatively small subset of genes can effectively characterize Cisplatin response in lung cancer, consistent with prior transcriptomic studies using large-scale pharmacogenomic resources such as CCLE [1] and GDSC [2].

C. Model Interpretation Using SHAP

To provide model-level interpretability and feature attribution, SHapley Additive exPlanations (SHAP) were applied. This method quantifies the contribution of each feature to individual predictions, offering a transparent view of the model's decision-making process [4].

The SHAP summary plot (Figure 2) highlights the genes with the strongest influence on Cisplatin response prediction.

In particular, SLFN11 exhibited the highest SHAP values, indicating a substantial impact on classification outcomes.

Higher expression levels of this gene were generally associated with an increased probability of drug sensitivity, consistent with its established biological role [9], [10]. Other genes, such as RAB22A and ITPRIPL1, also showed notable contributions, suggesting that multiple molecular pathways may be involved in determining Cisplatin response.

Importantly, the agreement between XGBoost feature importance rankings and SHAP-derived contributions reinforces the stability of the identified gene signature. This consistency suggests that the selected features represent reproducible biological signals rather than artifacts of a specific modeling approach.

The SHAP summary visualization is presented in Figure 2. To further contextualize the performance of the proposed framework, we compared our results with previously published studies employing machine learning models for cancer-related prediction tasks. It is important to note that prior studies do not address the exact same prediction task or data modality; rather, they provide relevant benchmarks for evaluating the effectiveness of ensemble learning methods in biomedical applications.

For example, Guan et al. (2023) developed an XGBoost- based model using metabolomic biomarkers for lung cancer prediction, reporting an accuracy of approximately 0.75 and an AUC of 0.81. While their study focused on early cancer detection using metabolic features, it similarly demonstrates the effectiveness of gradient boosting methods in high- dimensional biomedical data [14].

In contrast, the present study addresses drug response prediction of Cisplatin sensitivity using high-dimensional gene expression profiles derived from lung cancer cell lines. The proposed XGBoost model achieved an accuracy of approximately 0.79 and an ROC-AUC of 0.85, indicating competitive performance despite the increased complexity of transcriptomic data and drug response prediction tasks. Consistent with Table II, the proposed model achieves comparable or improved ROC-AUC values relative to metabolomic-based prediction frameworks [14], while addressing a more challenging prediction setting.

Furthermore, the proposed framework provides biologically interpretable insights through SHAP analysis, identifying key gene features such as SLFN11, which has been experimentally validated to modulate sensitivity to DNA- damaging agents, including platinum-based chemotherapy [9], [10]. The agreement between feature importance and SHAP-based interpretation further supports the robustness of the identified biomarkers.

Overall, these findings demonstrate that the proposed XGBoost-based framework achieves competitive predictive performance while additionally offering cross-dataset validation and biological interpretability, addressing both methodological rigor and practical relevance activity.

D. External Validation and Model Robustness

To further evaluate the robustness and statistical significance of the proposed model, additional experiments were conducted using an

independent external dataset that was not involved in the model development process.

The ROC curve obtained from the external validation dataset is presented in Figure 5. The model maintained strong discriminative performance, indicating its ability to generalize beyond the training and internal validation datasets.

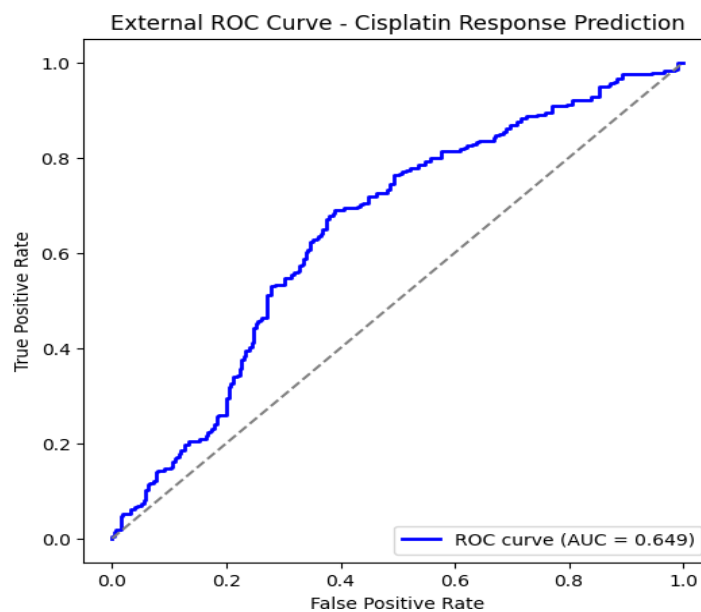


Fig. 5. External ROC Curve for Cisplatin Sensitivity

In addition to ROC analysis, a confusion matrix was generated to provide a detailed evaluation of classification performance. As shown in Figure 6, the model demonstrates a balanced ability to correctly classify both sensitive and resistant samples.

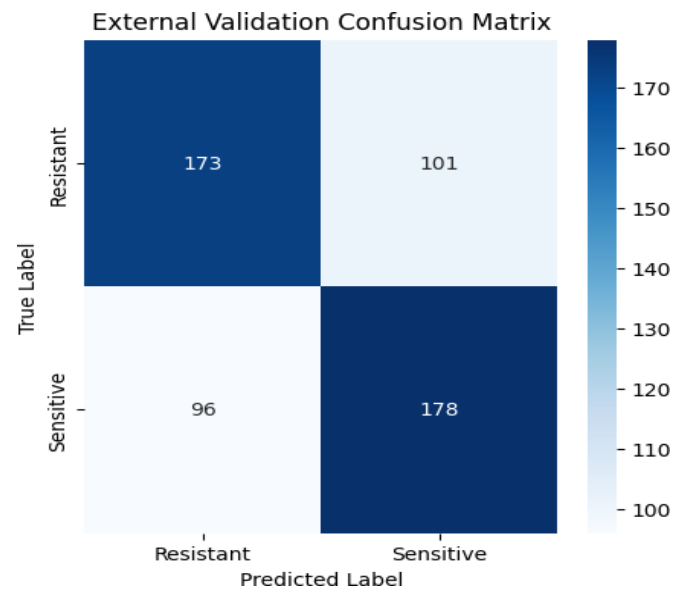


Fig. 6. External Validation Confusion Matrix

To further assess the statistical significance of the model performance, a permutation test was conducted. The distribution of AUC scores obtained from randomly permuted labels is shown in Figure 7. The original model performance lies significantly above the distribution of permutation scores, confirming that the predictive performance is not due to random chance.

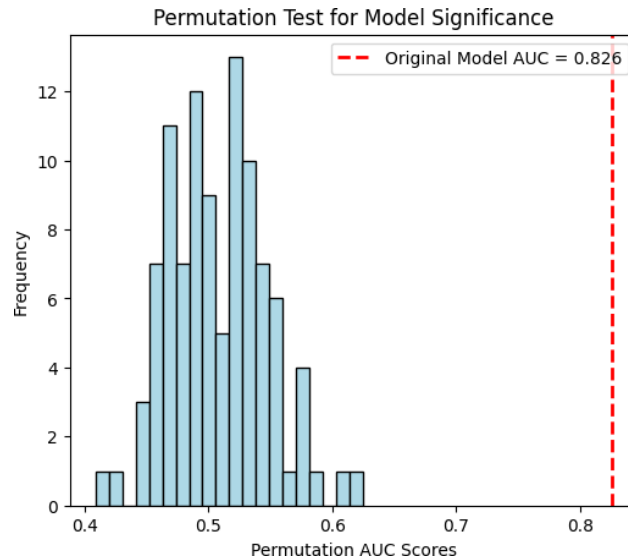


Fig. 7. Permutation Test for Model Significance

These results further support the robustness, generalizability, and statistical validity of the proposed XGBoost based framework.

IV. DISCUSSION

The results of this study demonstrate that machine learning models, particularly XGBoost, can effectively capture complex relationships between gene expression profiles and drug response in lung cancer cell lines. The proposed framework achieved strong predictive performance, with an ROC-AUC of 0.84 – 0.85, indicating its ability to discriminate between Cisplatin-sensitive and resistant samples.

A key strength of this study lies in the use of cross-dataset validation, where the model was trained on GDSC2 and evaluated on the independent GDSC1 cohort. This approach provides a more rigorous assessment of model generalizability compared to conventional validation strategies and suggests that the learned patterns are not limited to a single dataset.

The identification of biologically relevant genes, particularly SLFN11, further supports the validity of the proposed framework. Previous studies have shown that SLFN11 plays a critical role in sensitizing cancer cells to DNA-damaging agents, including platinum-based therapies [9], [10].

The agreement between XGBoost feature importance and SHAP-based interpretation reinforces the robustness of the selected gene signatures and highlights the potential of interpretable machine learning in uncovering meaningful biomarkers. In comparison with existing studies, the proposed model demonstrates competitive performance despite the increased complexity of transcriptomic data and drug response prediction tasks. Consistent with Table I, the proposed model achieves comparable or improved ROC- AUC values relative to metabolomic-based prediction frameworks [14], while addressing a more challenging prediction setting.

A. Clinical Relevance and Translational Potential

While our framework demonstrates robust predictive performance in lung cancer cell lines, its translation to patient tumors requires caution. The clinical utility of this model lies in its ability to provide a transparent, biomarker-driven decision support system. Unlike "black-box" models, the integration of SHAP values allows clinicians to understand the molecular rationale behind a sensitivity prediction, which is crucial for clinical adoption. Future studies should evaluate the identified gene signatures in clinical biopsy samples to determine their utility in guiding personalized Cisplatin therapy. Integrating this framework with clinical parameters, such as tumor stage and patient performance status, could further enhance its predictive power in a real-world oncology setting.

B. Biological Validation

The Experimental validation of the selected gene signature, particularly SLFN11, in clinical samples or patient- derived xenografts is necessary to confirm functional relevance and to support biomarker-driven treatment decisions. The consistent identification of SLFN11 across different interpretability methods suggests it could serve as a robust companion diagnostic marker for platinum-based regimens.

C. Methodological Considerations: Thresh holding and Sample Size

In this study, the median IC50 value was used as the threshold for binary classification, a common practice in pharmacogenomic modeling [6], [21]. While this ensures balanced classes, it may lead to the misclassification of samples with IC50 values near the median. Future research could explore alternative thresholding strategies, such as using the upper and lower quartiles (Q1 and Q4) to define extreme sensitive and resistant phenotypes, thereby increasing the molecular contrast between groups and potentially improving model discriminative power. Furthermore, although the sample size is limited relative to the high dimensionality of gene expression data, the use of external validation and cross- dataset testing reduces the risk of overfitting and supports the stability of our findings.

D. Generalizability

The framework could be adapted to predict responses to other chemotherapeutic agents or in different cancer types, provided appropriate pharmacogenomic datasets are available. Modifications may include retraining the model with drug-specific response data and revisiting feature selection strategies.

E. Feature Selection Robustness

Feature selection was performed using XGBoost importance scores, ensuring that selected genes contribute meaningfully to prediction. Alternative feature selection methods may be explored in future work. Overall, this study highlights the potential of integrating transcriptomic data with interpretable machine learning approaches to improve drug response prediction, while emphasizing the need for further validation in clinical and multi-omics settings.

V. CONCLUSION

In this study, we developed a robust machine learning framework for predicting Cisplatin response in lung cancer using high-dimensional gene expression data. Among the evaluated models, XGBoost demonstrated superior performance, achieving an accuracy of 0.79 and an ROC- AUC of 0.84, indicating a reliable predictive capability for drug sensitivity classification. A distinguishing feature of this framework is the integration of feature importance and SHAP analysis, which provides critical biological insights beyond simple prediction. By highlighting key genes such as SLFN11—which is strongly associated with response to DNA-damaging agents—the model bridges the gap between computational accuracy and biological interpretability.

This transparency is essential for the potential clinical adoption of AI-driven decision support systems in oncology. Furthermore, the inclusion of external validation using an independent dataset strengthens the robustness and generalizability of the findings, addressing a common limitation in many existing studies that rely solely on internal validation. Future work should focus on validating the model in clinical patient cohorts and experimentally confirming

the functional roles of the identified key genes to strengthen clinical applicability.

Incorporating multi-omics data may further enhance predictive performance and provide deeper biological insights. Overall, the proposed framework demonstrates significant potential for adaptation to additional drugs and cancer types, contributing to the development of more personalized and interpretable therapeutic strategies in precision oncology.

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