

RESEARCH ARTICLE

Chemical-Sensing Catheters for Long-Term and Personalized Therapeutic Management

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ABSTRACT

Long-term intravenous catheterization is vital for delivering chemotherapy to cancer patients and parenteral nutrition to those with intestinal failure, but it inevitably leads to complications, including metabolic disorders, bloodstream infection, liver injury, and kidney injury. Clinical monitoring methods show notable delays, while real-time blood monitoring devices fail to ensure long-term stability in vivo. Here, we present a chemical-sensing catheter that integrates multiple analyte sensors, including creatinine, taurocholic acid, bilirubin, and taurine, for real-time monitoring of complications in patients receiving long-term chemotherapy or parenteral nutrition in situ. The design of the metalgel preserves signal integrity through 1 million bending deformations, and a dual-network molecularly imprinted polymer suppresses in vivo performance degradation, enabling stable long-term operation of the chemical-sensing catheter over a 3 month implantation period. In chemotherapy and parenteral nutrition applications, early monitoring of liver and kidney injury, combined with prognostic intervention, mitigates risks such as bile stasis, hepatitis, and hepatic steatosis. With the integration of machine learning analysis of multimodal sensor data, this technology provides early prediction of complications and establishes a new paradigm for personalized therapeutic management.

1 | Introduction

Long-term intravenous catheterization is essential for life-saving interventions [1–3], delivering sustained chemotherapy to cancer patients and providing parenteral nutrition to those with intestinal failure [4, 5]. Annually, over 1 billion intravenous catheters are utilized worldwide [6], serving more than 9.8 million chemother-

apy patients and 50 million patients receiving parenteral nutrition [7, 8]. Prolonged infusion of drugs or nutrient solutions into the bloodstream by intravenous catheterization mainly lasts for 3 months [9], which inevitably leads to severe complications, including metabolic disorders, bloodstream infection, liver injury, and kidney injury [10–13]. This concern is underscored by high complication rates, reaching 48.1% in cancer patients and

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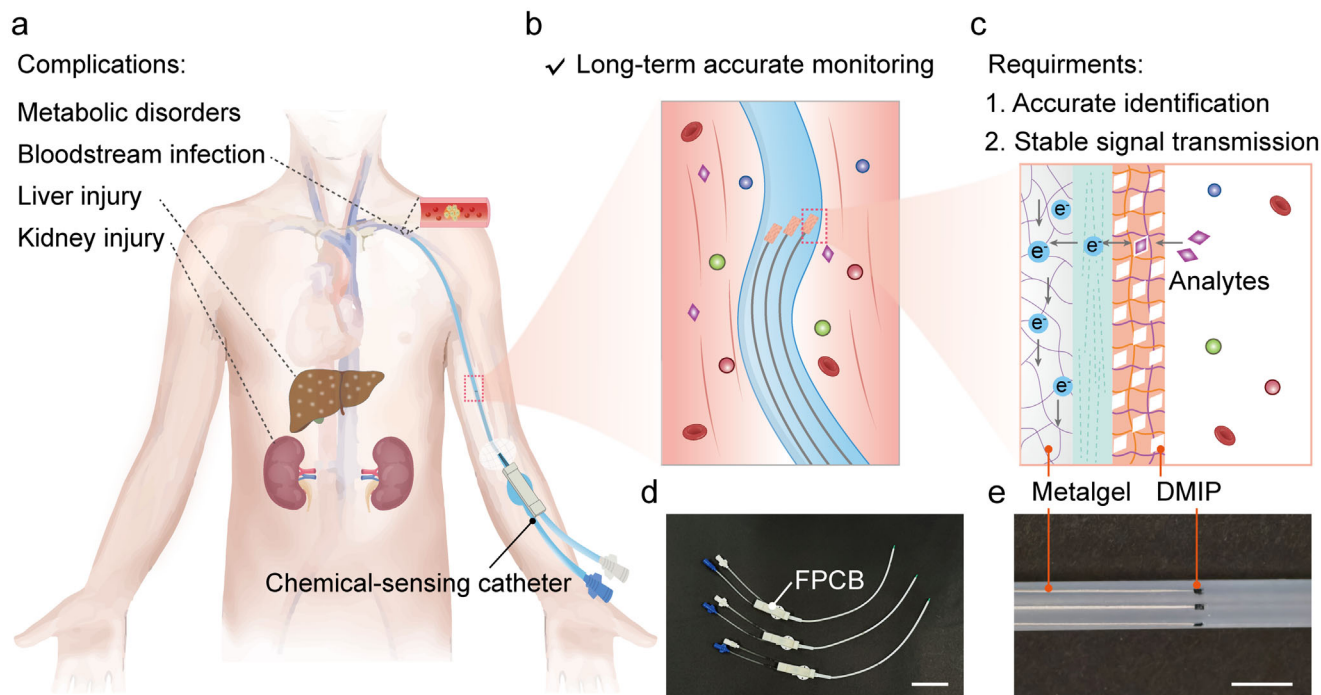


FIGURE 1 | Design of the chemical-sensing catheter for long-term and personalized management of complications. (a) Concept and design of chemical-sensing catheters for complications monitoring during chemotherapy and parenteral nutrition. Patients undergoing catheterization are prone to metabolic disorders, bloodstream infection, liver injury, and kidney injury. (b) The chemical-sensing catheter is developed to provide early warning of such complications by long-term, accurate monitoring. (c) The challenges of long-term monitoring are accurately identified in blood and stable signal transmission. (d,e) These functions are enabled by dual-network molecularly imprinted polymer (DMIP) and metalgel. Optical images of the chemical-sensing catheter are shown, including metalgel, DMIP, and flexible printed circuit board (FPCB). Scale bar, d: 5 cm; e: 2 mm.

39.6% in those receiving parenteral nutrition [14, 15], including hepatobiliary disorders with neonatal mortality exceeding 20.8% [16]. Current clinical monitoring approaches rely on periodic sampling with laboratory analysis [17], which is constrained by delayed processing leading to delayed diagnosis of complications, poor capture of disease progression dynamics, and the high cost of repeated testing [18–20].

Real-time monitoring tools for biomarker analytes have attracted considerable attention for early diagnosis of these diseases [21–23]. However, current biosensors largely depend on alternative biofluids such as sweat, saliva, or tears [24, 25], whose correlation with changes in the clinical gold standard of blood has not been demonstrated [26, 27]. Blood-based biosensors have begun to emerge, yet they require additional surgical implantation, and the biomarkers currently targeted lack associations with these complications [28–30]. Moreover, their monitoring windows are commonly restricted to 7–28 days, rendering them inadequate for the typical 3-month intravenous catheterization period required for continuous management [31, 32]. This highlights the need to develop blood-compatible sensing devices capable of accurate recognition, stable signal collection, and intelligent feedback over extended durations.

Here, we integrate biochemical sensors onto the surface of venous catheters, termed chemical-sensing catheters, thereby avoiding secondary implantation surgery of sensors and enabling long-term, accurate, and real-time monitoring of complications in patients undergoing chemotherapy and parenteral nutrition

(Figure 1a,b). This performance is attributed to a new dual-network molecularly imprinted polymer (DMIP), which enables accurate and sustained recognition of blood analytes, including creatinine, taurocholic acid, bilirubin, and taurine, whilst resisting massive protein and platelet adsorption (Figure 1c). The resulting electrical signals are transmitted through a soft metalgel with high conductivity and strong interfacial adhesion, ensuring stable signal delivery. This integrated system maintains stability after 3 months of implantation, ensuring continuous monitoring throughout the entire catheterization period. Benefiting from real-time and accurate monitoring of various key analytes, by applying machine learning to multimodal sensor data, we achieve early warning of patient-specific complication trajectories. These advances establish a new paradigm for real-time intravascular monitoring, with implications for personalized management of patients needing long-term catheterization.

2 | Results and Discussion

2.1 | Design of the Chemical-Sensing Catheter

Constructing such a biochemical sensing catheter in blood presents the following challenges: (i) maintaining high sensitivity and accuracy whilst resisting massive protein and platelet adsorption throughout implantation periods up to 3 months; (ii) ensuring reliable signal transduction through a million deformations generated by physiological movements.

To address these challenges, we developed the chemical-sensing catheter integrating metalgel interconnects, DMIP, and a flexible printed circuit board (FPCB) for long-term, accurate blood monitoring (Figure 1d). Metalgel interconnects were printed precisely onto the catheter surface along the infusion direction and encapsulated in polydimethylsiloxane (PDMS) (Figure S1). This printing approach enabled customizable fabrication of up to 10 distinct conductive pathways per catheter, accommodating diverse monitoring requirements. The flexible polymer network interpenetrating the metalgel firmly anchored the metallic phase, thereby enabling the conductive pathways to acquire exceptional deformation resistance.

The sensing layers were constructed by depositing DMIP, combining antifouling zwitterionic polymers with specifically recognizing molecularly imprinted polymers, onto carbon nanotube (CNT) films (Figure 1e). These functionalized films simultaneously resisted nonspecific adsorption of proteins and platelets while enabling selective detection of clinically key analytes, including creatinine, taurocholic acid, bilirubin, and taurine. These films were adhered to metalgel circuit termini, thereby establishing robust electrical and mechanical interfaces. The thickness of the chemical-sensing layer was approximately 80 μm , which was merely 5% of a standard venous catheter's diameter. This integrated sensing system preserved the catheter's clinical functionality without compromising fluid dynamics or patient comfort.

The silicone-encapsulated FPCB ($1 \times 5 \times 0.5 \text{ cm}^3$), attached to the catheter's Y-connector positioned outside the patient, provided programmable voltage scanning from -1 to $+1 \text{ V}$ for electrochemical sensing. The FPCB acquired sensor signals via the metalgel interconnects and wirelessly transmitted data to mobile devices through Bluetooth connectivity (Figures S2 and S3). These features enabled continuous, real-time patient monitoring.

2.2 | The Metalgel for Stable Signal Transmission

Conventional conductive adhesives, such as silver pastes, carbon tape, copper tape, and nickel tape, exhibit cracking-induced fracture when subjected to millions of deformations generated by physiological movements [33]. Moreover, these conductive adhesives show limited interfacial adhesion performance under long-term blood flush, leading to delamination and significant signal attenuation during in vivo transmission (Figure 2a).

For stable signal transmission, we developed a flexible, conductive, and strongly adhesive metalgel by immobilizing a liquid metal continuum within a waterborne polyurethane-sorbitol network. The metalgel was 3D-printed on the catheter surface (Figures S4 and S5) and formed a linear array that enabled multiplexed signal transmission (Figure 2b). During the printing process, heating induced water evaporation from the slurry and anisotropic volume shrinkage. The waterborne polyurethane (WPU) polymers formed a uniformly entangled 3D network with an average pore size of 7.4 μm , as revealed by micro-computed tomography (micro-CT) images (Figures 2c and S6a). Sorbitol molecules responsible for adhesion migrated with evaporating water to the material surface (Figures 2e and S7), thereby enabling

the formation of adhesive interfaces. Concurrently, compressive stress derived from this contraction interconnected liquid metal droplets into a continuum within the polymer network to establish conductive pathways, as demonstrated by the uniform distribution of Ga in the cross-sections of the scanning electron microscope (SEM) images and the interconnected continuity shown in the micro-CT images (Figures 2d and S6b).

Thermogravimetric analysis revealed that the liquid metal content of the metalgel was 94% (Figure S8). Correspondingly, the metalgel exhibited metallic-level electronic conductivity of $2.1 \times 10^6 \text{ S}\cdot\text{m}^{-1}$ with tightly clustered conductivity distribution and homogeneity (Figure S9). In addition, nanoindentation measurements showed the Young's modulus of 702.37 kPa (Figure S10), reflecting the compliant mechanical nature of the metalgel. During 1 million bending cycles, electrostatic interaction between WPU and liquid metal (Figure S11) enabled deformation of the liquid metal within the polymer network, thereby ensuring persistent conductive pathways and virtually unchanged conductivity (Figure S12). In contrast, commercial silver pastes exhibited cracking-induced failure when subjected to fewer than 10% of the bending cycles (Figure 2f). Compared with previously reported liquid-metal/polymer composite gels [34–38], which feature dispersed liquid-metal droplets in a hydrogel matrix (water as the fluid phase) with metal loadings below $\sim 20 \text{ wt}\%$ and conductivities of $10^{-2} \sim 10^3 \text{ S}\cdot\text{m}^{-1}$, the metalgel adopts a continuous liquid-metal phase with liquid metal as the fluid phase, stabilized by the polymer network. This enables $>90 \text{ wt}\%$ metal content to be present in the gel, achieving a percolated conductive network throughout the gel, as well as exceptional mechanical durability.

A stable interface between the sensing layer and the metalgel was also critical for reliable signal transmission. Sorbitol, a small molecule containing multiple hydroxyl groups, migrates to the metalgel surface during solvent evaporation. This results in the formation of dense hydrogen-bonding interactions between the metalgel and the carboxylated carbon nanotube film, effectively coupling the two components (Figure S13). When the mass ratio of sorbitol to WPU reached 0.8, a maximum adhesion toughness of $217.17 \text{ J}\cdot\text{m}^{-2}$ was achieved (Figure S14). This interfacial engineering strategy outperforms conventional liquid metal-elastomer adhesion approaches, which typically suffer from low interfacial enrichment [39–44] with adhesive groups dispersed in the bulk, leading to limited adhesion ($<100 \text{ J}\cdot\text{m}^{-2}$). Besides, in traditional droplet-based liquid metal-elastomer composites, the discrete metal domains disrupt conductive pathways, severely limiting electrical conductivity to $10^{-2} \sim 10^3 \text{ S}\cdot\text{m}^{-1}$.

Notably, following 30 days of simulated blood exposure with a bending radius of 5 mm and a flow rate of $40 \text{ cm}\cdot\text{s}^{-1}$, the metalgel maintained an adhesion toughness of $176.55 \text{ J}\cdot\text{m}^{-2}$. In contrast, commercial conductive tapes, including carbon tape, silver paste, copper tape, and nickel tape, demonstrated a reduction in adhesion toughness to below $100 \text{ J}\cdot\text{m}^{-2}$ within 15 days (Figure 2g). This adhesion stability of the metalgel was attributable to sorbitol-mediated hydrogen bonding networks that bridged the 3D polymer network and the sensing layer, thereby creating a structurally unified interface. Conversely, commercial laminated structures suffered from weak adhesive interfaces, leading to accelerated interfacial failure upon moisture

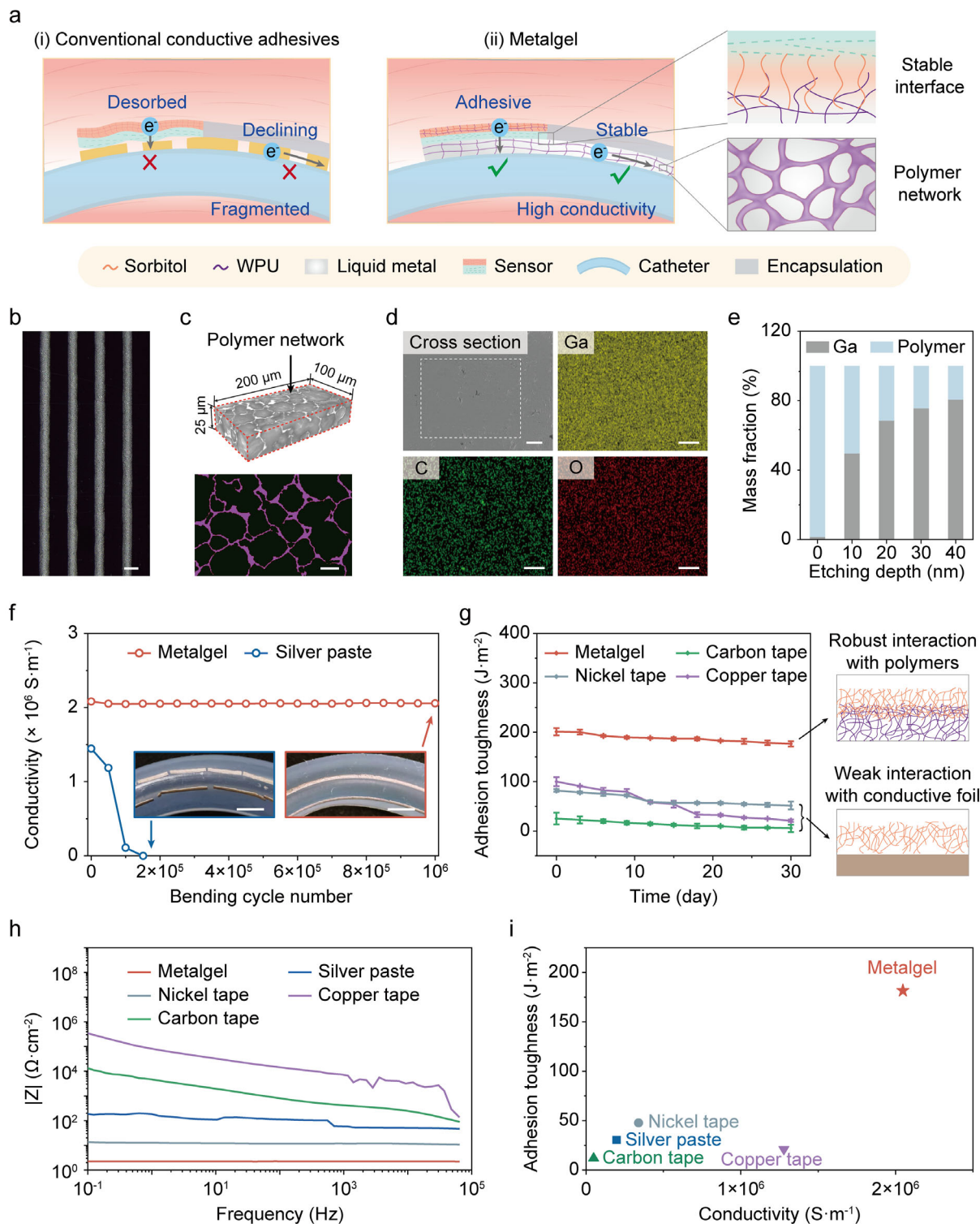


FIGURE 2 | Structure and performance of metalgel. (a) Schematic illustration of the comparison between traditional commercial adhesives and metalgel. Metalgel has a deformable gel network and a stable interface with sensors. (b) Optical photograph of metalgel circuits. Scale bar, 200 μm . (c) Three-dimensional reconstructed microstructure of the metalgel and the cross-sectional view of the polymer network, both of which were obtained from micro-computed tomography. Scale bar, 10 μm . (d) Scanning electron microscope (SEM) and energy dispersive spectrometer (EDS) elemental mapping images of the metalgel. Scale bar, 10 μm . (e) Mass fractions of Ga and polymer in the metalgel at etching depths of 0–40 nm calculated by X-ray photoelectron spectroscopy (XPS) spectra. (f) Relative conductivity changes and optical photographs of metalgel and commercial conductive adhesives during 10^6 bending cycles. Scale bar, 1 cm. (g) Adhesion toughness evolution between different conductive adhesives and sensing layers for 30 days in a simulated venous environment (bending radius: 5 mm, flow rate: 30–40 $\text{cm}\cdot\text{s}^{-1}$). Values are the mean $\pm$ SD for $n = 3$ samples. (h) Comparison of interface impedance between metalgel/commercial conductive adhesives and sensing layer after 30 days in a simulated venous environment (bending radius: 5 mm, flow rate: 30–40 $\text{cm}\cdot\text{s}^{-1}$). (i) Ashby-style plot comparing the surface electrical conductivity and adhesion toughness of metalgel to commercial conductive adhesives.

exposure. The metalgel's robust interfacial adhesion also enabled strong bonding to catheter substrates, facilitating seamless integration of the chemical-sensing catheter (Figure S15). Owing to the metalgel's long-term durability in electrical conductivity and interfacial adhesion performance, the metalgel-sensing layer interface demonstrated an ultralow impedance of $2.24 \Omega \cdot \text{cm}^{-2}$ at 0.1 Hz, less than 10% of that in conventional conductive adhesives (Figure 2h). The metalgel exhibited metallic conductivity and conformal interfacial bonding arising from its structural design, showing 4–15-fold enhanced interfacial adhesion compared with existing conductive adhesives. The surface conductivity of the metalgel was approximately 2- and 40-fold higher than that of copper tape and carbon tape, respectively. This performance difference primarily arises from variations in surface structure and bulk conductivity (Figure 2i).

2.3 | The DMIP for Long-Term High-Sensitivity Sensing

In complex blood environments, long-term continuous monitoring of specific biomarkers faces significant challenges due to surface contamination, which leads to rapid deterioration of sensor performance and ultimately fails to meet practical application requirements [26, 45]. To address this issue, a common approach involves coating the sensor surface with antifouling layers to inhibit biological adhesion. Although this strategy mitigates biofouling, the antifouling coating obscures electrochemically active sites and increases the diffusion resistance of analytes, thereby substantially compromising the sensor's sensitivity and detection limit.

We developed a new sensing material based on a dual-network molecularly imprinted polymer (Figure 3a). This sensing material was constructed as an interpenetrating network through the integration of poly(o-aminophenol) (POAP) and poly(sulfobetaine methacrylate) (PSBMA). Fourier transform infrared (FTIR) spectroscopy confirmed the successful synthesis of the DMIP, as evidenced by the simultaneous presence of the characteristic C=O stretching vibration peak from PSBMA and the aromatic C=C stretching vibration peak from POAP (Figure S16a, b). Energy-dispersive spectroscopy mapping further revealed a homogeneous distribution of characteristic elements such as nitrogen and sulfur, indicating uniform dispersion of the two polymers (Figure S16c). The DMIP enabled the formation of precise binding sites, allowing highly selective recognition of target biomarkers such as creatinine molecules (Figure 3b). Evaluation of the sensing performance within the physiological concentration range of creatinine (Figure S17a) demonstrated a strong linear relationship between the sensor's peak current and creatinine concentration, with a sensitivity of $33.54 \mu\text{A} \cdot \text{dec}^{-1}$ (Figure S17e), along with excellent reproducibility (Figure S17i). The detection limit of the creatinine sensor was calculated to be $1.72 \mu\text{M}$, outperforming conventional Jaffe and enzymatic assays, which typically exhibited detection limits of $4.4\text{--}8.8 \mu\text{M}$ [46, 47].

To validate the response performance of the DMIP sensor of creatinine in vivo, the sensor was implanted into rats, which showed less than 2% attenuation in peak current after 3 months of implantation (Figure S18d–f). The sustained superior performance of DMIP sensor of creatinine in vivo was attributed to the synergistic

electrostatic interaction between positively charged groups ($-\text{NH}_2$) and negatively charged groups ($-\text{SO}_3\text{H}$), coupled with surface hydrophilicity (rich in polar functional groups such as $-\text{NH}_2$ and $-\text{OH}$), which collectively facilitated the formation of an interface with strong surface hydration capacity (Figure S19) [48]. This interface effectively promoted the formation of a hydration layer, thereby suppressing biofouling accumulation. Protein and platelet adhesion experiments further confirmed the exceptional antifouling properties of this interface, with adhesion rates of fibrinogen (FBG) and platelets remaining below 5% and 15%, respectively (Figure 3c). Consistently, comparative tests in porcine whole blood before and after 3 months showed no obvious degradation (Figure S20) or swelling (Figure S21) of the DMIP. Moreover, after 3 months of implantation in rats, no significant protein adsorption or material degradation was observed (Figures S22).

Importantly, while maintaining outstanding antifouling performance, the hydration layer of DMIP did not compromise the sensor's response characteristics (Figures 3e and S18a–c). It is worth noting that molecularly imprinted polymer (MIP) sensors of creatinine and antifouling-coated MIP sensors of creatinine were used as control groups. After 3 months of implantation, the peak current of MIP sensors decreased to 19.06% of the initial value due to biofouling. By contrast, MIP sensors modified with conventional antifouling coatings exhibited a significantly lower initial peak current, reaching only 32.05% of that of DMIP sensors. This was mainly due to the partial shielding of the imprinted recognition sites and reduced accessibility of the analytes (Figure S18d–f). These results further highlighted the advantages of the DMIP design. The DMIP sensor of creatinine exhibited in vivo creatinine detection stability of 96.45% over 3 months, whereas the MIP sensor retained only 6.16% (Figures 3d–f and S23a, b). The DMIP sensor of creatinine also exhibited a selective response to common interfering biochemical substances in blood, including glutamic acid, amino acids, uric acid, serine, and lactic acid (Figure 3g).

Moreover, the DMIP design of the creatinine (CR) sensor was extended to other clinically relevant blood biochemical markers, including taurocholic acid (TCA), bilirubin (BIL), and taurine (TAU). Within the physiological concentration range (Figure S17a–d), the sensitivities of creatinine, taurocholic acid, bilirubin, and taurine were $33.54 \mu\text{A} \cdot \text{dec}^{-1}$, $0.925 \mu\text{A} \cdot \text{dec}^{-1}$, $0.097 \mu\text{A} \cdot \mu\text{M}^{-1}$, and $23.85 \mu\text{A} \cdot \text{dec}^{-1}$, respectively (Figure S17e–h). After 3 months of implantation, the 4 sensors maintained stable performance, exhibiting low baseline drift values of 1.27%, 3.90%, 2.32%, and 4.10%, respectively (Figures S23 and S24). These sensors also maintained good selectivity in the presence of common interfering biochemical substances in blood (Figure S25). Furthermore, the recognition performance of DMIP sensors was maintained across different environments, including lipemic serum and in the presence of drug metabolites (Figure S26). The DMIP sensors also showed consistent responses when tested under simulated in vivo conditions involving various flow velocities, pH levels, ionic strengths, and serum matrices (Figures S27–S30).

2.4 | Performance of the Chemical-Sensing Catheter

Benefiting from the design of the metalgel interconnects and DMIP sensing interface, the device had maintained consistent

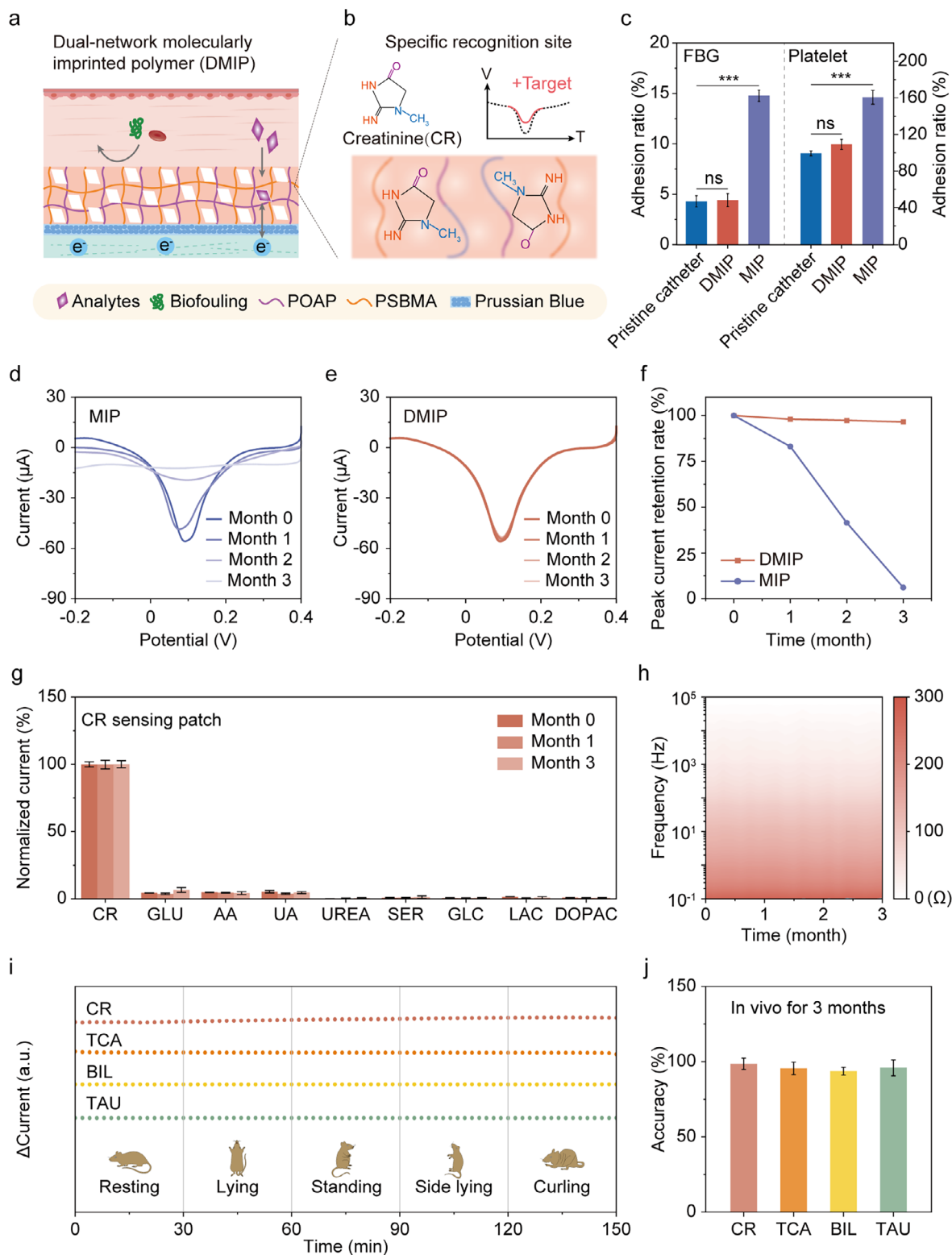


FIGURE 3 | Structure and sensing performance of DMIP. (a) Schematic illustration of the DMIP's structure. (b) Schematic illustration of the DMIP's specific recognition principle. (c) Comparison of the adhesion of fibrinogen (FBG) and platelet by MIP group, DMIP group, and pristine catheter. Values are the mean $\pm$ SD for $n = 3$ samples. ns, no significant difference. $*p \leq 0.05$, $**p \leq 0.01$, and $***p \leq 0.001$. (d,e), Creatinine (CR) response curve of sensing patches with MIP (d) and with DMIP (e) in simulated blood after being implanted in rats for 1 to 3 months, along with their corresponding peak current retention rates. (f) Stability of peak current retention rate over the course of a 3-month incubation in simulated blood for sensing patches with MIP and with DMIP. (g) Selectivity measurement of CR sensing patch for Month 0, 1, and 3. Values are the mean $\pm$ SD for $n = 3$ samples. (h) The impedance magnitude changes of a sensing patch from the chemical-sensing catheter for 3 months. (i) The signal stability of the chemical-sensing catheter in rats across various postures, including resting, lying, standing, side lying and curling. (j) The accuracy of CR, taurocholic acid (TCA), bilirubin (BIL) and taurine (TAU) for 3 months in vivo compared with standard testing (ELISA detection kits). Values are the mean $\pm$ SD for $n = 3$ samples.

impedance throughout the 3-month testing period (Figures 3h and S31a, b). In addition, the chemical-sensing catheter exhibited less than 4.49% signal fluctuation across various rat postures, including standing, lateral recumbency, and curling (Figure 3i). A comparison between the monitoring results obtained 3 months after *in vivo* catheter implantation, and those from standard laboratory blood analyses showed good agreement, with accuracies of 98.27% for the CR sensor, 95.32% for the TCA sensor, 93.71% for the BIL sensor, and 95.88% for the TAU sensor (Figures 3j, S23c, and S32).

DMIP sensors enabled continuous *in vivo* detection through *in situ* electrochemical regeneration. After detection, a predefined constant potential (equal to the negative value of the response peak potential) was applied to the chemical-sensing catheter. This induced electrostatic repulsion, releasing charged analytes from the imprinted sites and restoring their binding capability. Electrochemical impedance analysis of the charge-transfer resistance further confirmed the reversibility of analyte binding and desorption. Importantly, regeneration refers to the restoration of binding-site availability, whereas calibration describes the stability of the concentration–signal relationship over time. During continuous testing in simulated blood, DMIP sensors retained their initial current responses after more than 260 consecutive “detection-*in situ* electrochemical regeneration” cycles (Figures S33–S36). After 3 months of implantation, the electrochemical response curves of the sensing catheter fully recovered to their initial states after regeneration, with recovery rates consistently exceeding 96.6% (Figures S37–S41). This demonstrated that the electrically driven regeneration mechanism remained effective under physiological conditions.

The reliability and biocompatibility of the chemical-sensing catheter were investigated. *In vitro* cell culture experiments and hemolysis tests indicated that the material had minimal impact on cell viability (Figure S42) and did not induce significant hemolysis under the tested conditions (Figure S43). The encapsulated metalgel interconnects on the chemical-sensing catheter showed no noticeable changes after 3 months of implantation (Figure S44a), and their electrical resistance remained stable (Figure S44b). Color Doppler ultrasound imaging and blood flow velocity measurements revealed no thrombus formation at either 1 week or 3 months post-implantation (Figure S31c, d). In addition, the serum Ga^{3+} concentration measured after 3 months of implantation was $2.83 \mu\text{g}\cdot\text{L}^{-1}$, remaining comparable to the initial level (Figure S44c), while the cumulative leaching percentage of residual monomers from the MIP components remained at a low level below 3.9%. Hematological analysis during the same period showed no significant differences in white blood cell/red blood cell counts, hemoglobin levels, or mean platelet volume (Figure S31e, f), indicating that the device exhibited good hemocompatibility under the tested conditions. Prothrombin time (PT) and activated partial thromboplastin time (APTT) in the plasma of the experimental group were comparable to those in the control group (Figure S45), indicating no significant abnormalities in coagulation. Histological analysis by hematoxylin and eosin (H&E) staining and immunofluorescence staining revealed no abnormal immune activation in the surrounding vascular tissues, indicating good tissue integration (Figure S46). Furthermore, H&E staining of major organs revealed no pathological changes, confirming the absence of systemic toxicity (Figure S47).

2.5 | Application in Chemotherapy

Chemotherapy is the primary modality in cancer treatment. However, most cancer patients suffer from chemotherapy-related complications [5, 15]. The major complications are liver injury and kidney injury, which severely impact patients' quality of life and increase mortality risk (Figure 4a). Therefore, in addition to improving survival rates, the early monitoring and timely intervention of chemotherapy complications in the cancer care setting is imperative. Creatinine, taurocholic acid, bilirubin, and taurine are clinically relevant biomarkers of early renal and hepatic dysfunction during chemotherapy, and are commonly used to reflect organ injury in routine clinical evaluation [49].

Using cisplatin as a model chemotherapeutic agent, we demonstrated the catheter's ability to continuously track blood creatinine concentrations during drug-induced renal failure. As shown in Figure 4b, after cisplatin administration, creatinine levels increased rapidly and reached a peak of $113.98 \mu\text{M}$ at 100 h, which was approximately 2.5 times higher than normal. At peak creatinine concentration, renal tissues were harvested for terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) fluorescence staining analysis. The results indicated evident renal toxicity, with TUNEL fluorescence intensity markedly higher than that in the pristine catheter group (Figure 4c, d). Notably, while conventional clinical examinations were typically performed every 3 weeks [50], our catheter detected abnormalities and issued warnings in time, providing a critical window for intervention. This continuous monitoring enables earlier detection than intermittent laboratory testing by capturing rapid biomarker transitions that may be missed between clinical visits, allowing intervention during the early stage of organ injury before overt clinical manifestation and improving the potential for reversible outcomes.

To evaluate hepatic injury monitoring, the chemical-sensing catheter was used to track the dynamic changes in blood taurine and bilirubin levels following cyclophosphamide administration. As shown in Figure 4e, both biomarkers exhibited rapid change following injection, with taurine declining from 1.13 to $0.51 \mu\text{M}$ and bilirubin rising from $5.33 \mu\text{M}$ to $11.96 \mu\text{M}$ at 30 h. Timely intervention prompted by chemical-sensing catheter alerts restored bile acid and triglyceride levels to normal (Figure 4f). In contrast, rats without an alert developed early-stage hepatitis (Figures 4g and S48). Altered expression of the hepatic genes, including acetyl-CoA carboxylase 1 (ACC1) and sterol regulatory element-binding protein 1c (SREBP-1c), further confirmed the protective effect of the early warnings (Figure 4h). These results demonstrated that the chemical-sensing catheter enabled the early detection of hepatic and renal injury and facilitated timely intervention, thereby reducing the risk of chemotherapy-associated complications such as renal failure and hepatic fibrosis.

The implications of this technology extend beyond toxicity monitoring. As a proof of concept, the chemical-sensing catheter was capable of monitoring changes in the concentration of the neuroblastoma biomarker vanillylmandelic acid within the physiological range ($10\text{--}100 \mu\text{M}$), with a sensitivity of up to $0.11 \mu\text{A}\cdot\mu\text{M}^{-1}$. This enabled continuous, real-time tracking of vanillylmandelic acid fluctuations in rat models (Figure S49).

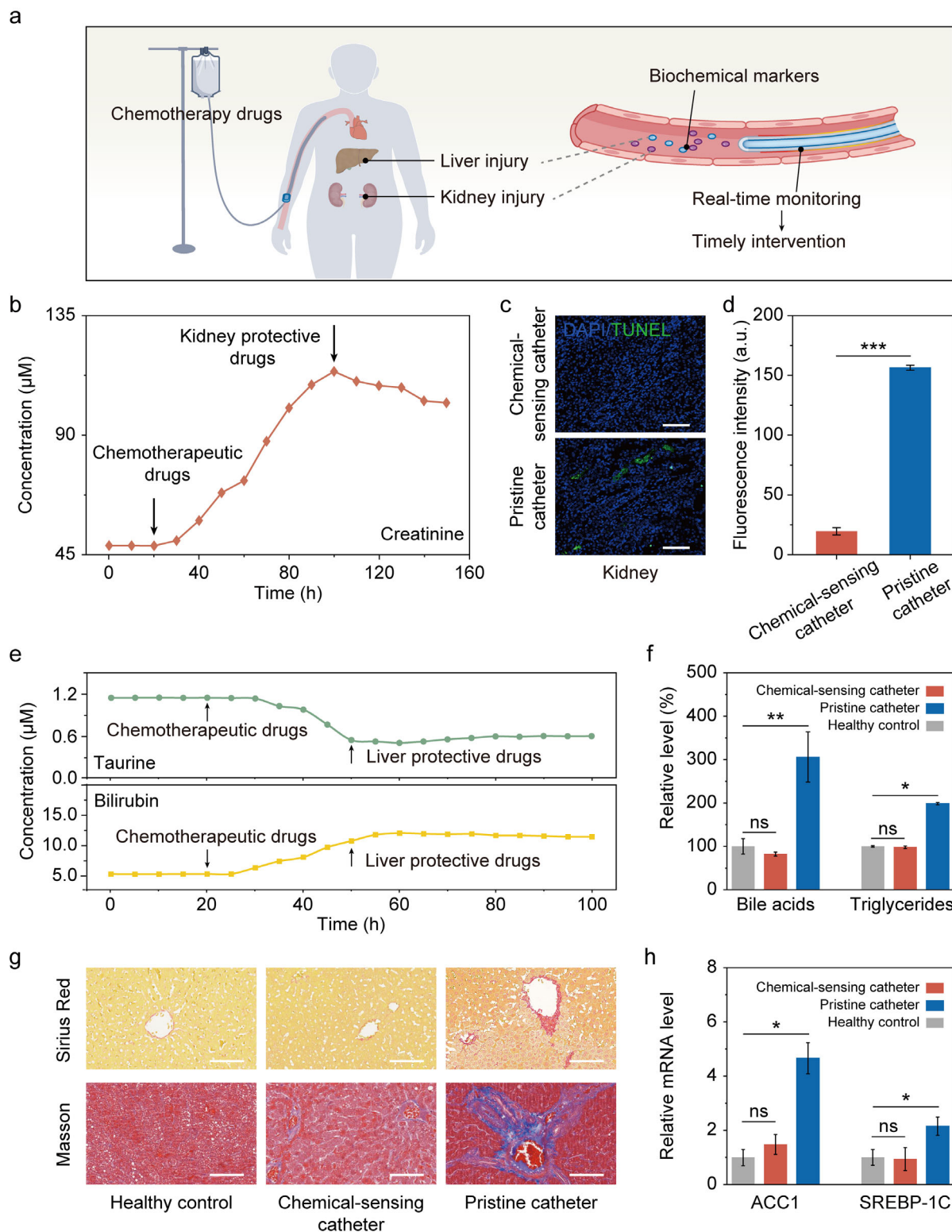


FIGURE 4 | Application of the chemical-sensing catheter in chemotherapy. (a) Schematic illustration of the chemical-sensing catheter monitoring and early warning of biochemical markers. (b) In vivo monitoring of blood creatinine concentrations during different periods of renal injury. (c) Representative TUNEL fluorescence images of the pristine catheter group and the chemical-sensing catheter group. Scale bar, 100 μm . (d) Statistical analysis of fluorescence intensity from c. Values are the mean $\pm$ SD for $n = 3$ rats. (e) In vivo monitoring of blood taurine and bilirubin concentrations during different periods of liver injury. (f) Relative levels of bile acids and triglycerides in the pristine catheter group, chemical-sensing catheter group, and healthy control group. Values are the mean $\pm$ SD for $n = 3$ rats. (g) Sirius Red and Masson's trichrome staining images of liver sections from the pristine catheter group, the chemical-sensing catheter group, and the healthy control group. Scale bar, 100 μm . (h) Relative mRNA expressions of ACC1 and SREBP-1C in the pristine catheter group, chemical-sensing catheter group and healthy control group. Values are the mean $\pm$ SD for $n = 3$ rats. All data presented as mean $\pm$ SD. ns, no significant difference. $*p \leq 0.05$, $**p \leq 0.01$, and $***p \leq 0.001$.

In the future, chemical-sensing catheters may enable real-time tracking of cancer cell clearance during treatments for hematologic malignancies, choriocarcinoma, and testicular cancer, thereby supporting precision drug administration and accelerating clinical cure. For patients with solid tumors undergoing adjuvant chemotherapy following surgery or radiotherapy, continuous monitoring of minimal residual disease biomarkers could optimize treatment schedules while minimizing the risk of recurrence.

2.6 | Application in Parenteral Nutrition

Patients receiving parenteral nutrition are another group who depend on intravenous catheters, as they require nutrient infusion due to the inability to ingest or absorb food orally [4]. This therapy is commonly used for patients with severe gastrointestinal dysfunction, chronic intestinal failure, and for those recovering from surgery, serving as their sole source of essential calories and micronutrients [51]. However, long-term dependence on intravenous nutrition makes achieving metabolic balance particularly critical. Substantial inter-individual variability in metabolic demands and nutrient utilization limits the effectiveness of standardized regimens [52]. Differences in electrolyte turnover, trace element metabolism, and vitamin requirements often result in either subclinical deficiencies or toxic accumulation despite adherence to guideline-based formulations. Such variability limits the effectiveness of standardized nutritional plans and increases the risk of associated complications, including metabolic, hepatobiliary, and catheter-related complications [14, 53].

The chemical-sensing catheter integrates multi-analyte detection with machine learning algorithms to assess complication risk in patients receiving parenteral nutrition. This system enables real-time risk stratification and therapeutic optimization, representing a paradigm shift toward precision medicine in parenteral nutrition management (Figure 5a). We selected five clinically representative complication states (liver damage, hypercalcemia, hyperkalemia, inflammation, and normal) as the target outcomes. The chemical-sensing catheter monitored five analytes (K^+ , Ca^{2+} , H_2O_2 , BIL, and TAU). Previous results indicated that BIL and TAU showed marked changes under liver injury (Figure 4e), while Ca^{2+} , K^+ , and H_2O_2 exhibited significant variations in metabolic complications and inflammation (Figures S50–S56). These biomarkers, however, were not specific to a single pathology, making integrated analysis essential to achieve reliable discrimination. We applied k-means clustering to 1500 datasets from 25 SD rats across the five states (Figure 5b). The data formed distinct clusters matching the clinical categories with an accuracy of 98.80%, demonstrating the strong discriminative capacity of the selected features (Figure S57). Building on this result, we constructed a backpropagation (BP) neural network for complication state classification. The model, designed with 5 input neurons, 10 hidden neurons, and 5 output neurons was trained on 80% of the dataset. After 100 epochs, the training process reached convergence with stable accuracy and loss curves, and the test accuracy reached 99.00% (Figure 5c, d), with the F1 score and area under the receiver operating characteristic curve (AUC–ROC) of the BP neural network reaching 99.16% and 1, respectively. The remaining 20% of the data were used for independent

validation, yielding a prediction accuracy of 99.33% (Figure S58). These results demonstrated that the chemical-sensing catheter, combined with machine learning, provided a robust and reliable health evaluation system for parenteral nutrition management.

The proposed health evaluation system was further applied to assess the status of parenteral nutrition-related complications. 10 SD rats received standardized parenteral nutrition, and daily feature signals were continuously collected and analyzed. After 7 days, different assessed results were observed among the rats, with 5 rats maintaining normal physiology, 3 developing inflammatory responses, 1 showing hyperkalemia, and 1 presenting hepatic dysfunction (Figure 5e). This distribution highlighted substantial individual variability under identical nutritional regimens, which was consistent with the heterogeneity commonly observed in clinical practice. In a representative case, the assessed risk profile of sample-A showed a progressive increase in hyperkalemia probability from Day 1 to 7 (Figure 5f), indicating that the system could dynamically capture the onset and progression of pathological changes. To validate the assessment, TUNEL staining images of the heart on day 7 revealed cardiomyocyte apoptosis (Figure 5g), and Kidney Injury Molecule-1 (KIM-1) fluorescence staining images of the kidney indicated impaired renal filtration (Figure 5h), together providing evidence of hyperkalemia (Figure S59). Importantly, if chemical-sensing catheter-based monitoring had been applied in practice, an optimized potassium nutritional plan could have been initiated on Day 3, enabling intervention at least 4 days earlier than the manifestation of clinical symptoms.

These results highlighted not only the effectiveness of the proposed health evaluation system but also its translational potential in clinical practice (Figure S60). In patients reliant on long-term parenteral nutrition, continuous biochemical surveillance could provide early warnings of hepatic dysfunction or electrolyte imbalance, allowing clinicians to intervene before irreversible organ damage occurs. For individuals requiring home-based parenteral nutrition, real-time remote monitoring of nutritional status could guide timely regimen adjustments and reduce the burden of frequent hospital visits. By integrating continuous chemical-sensing with intelligent data analysis, the catheter system transforms parenteral nutrition from a static, risk-prone intervention into a dynamic, feedback-driven therapy. Such a closed-loop strategy promises to lower complication rates, extend the safe duration of parenteral nutrition support, and accelerate the shift from population-based nutritional guidelines to truly personalized, precision nutrition within the broader framework of digital health.

3 | Conclusion

Our chemical-sensing catheter represents a convergence of advanced materials science and biomedical engineering to address fundamental challenges in continuous health monitoring. The integration of the durable, conductive metalgel and DMIP layers in the catheter overcomes two long-standing, critical challenges of implantable biosensors: unstable signal transmission and biofouling-induced performance degradation. This materials-driven approach establishes a versatile platform technology that can be adapted to various in vivo sensing applications, offering a pathway toward reliable long-term biochemical monitoring.

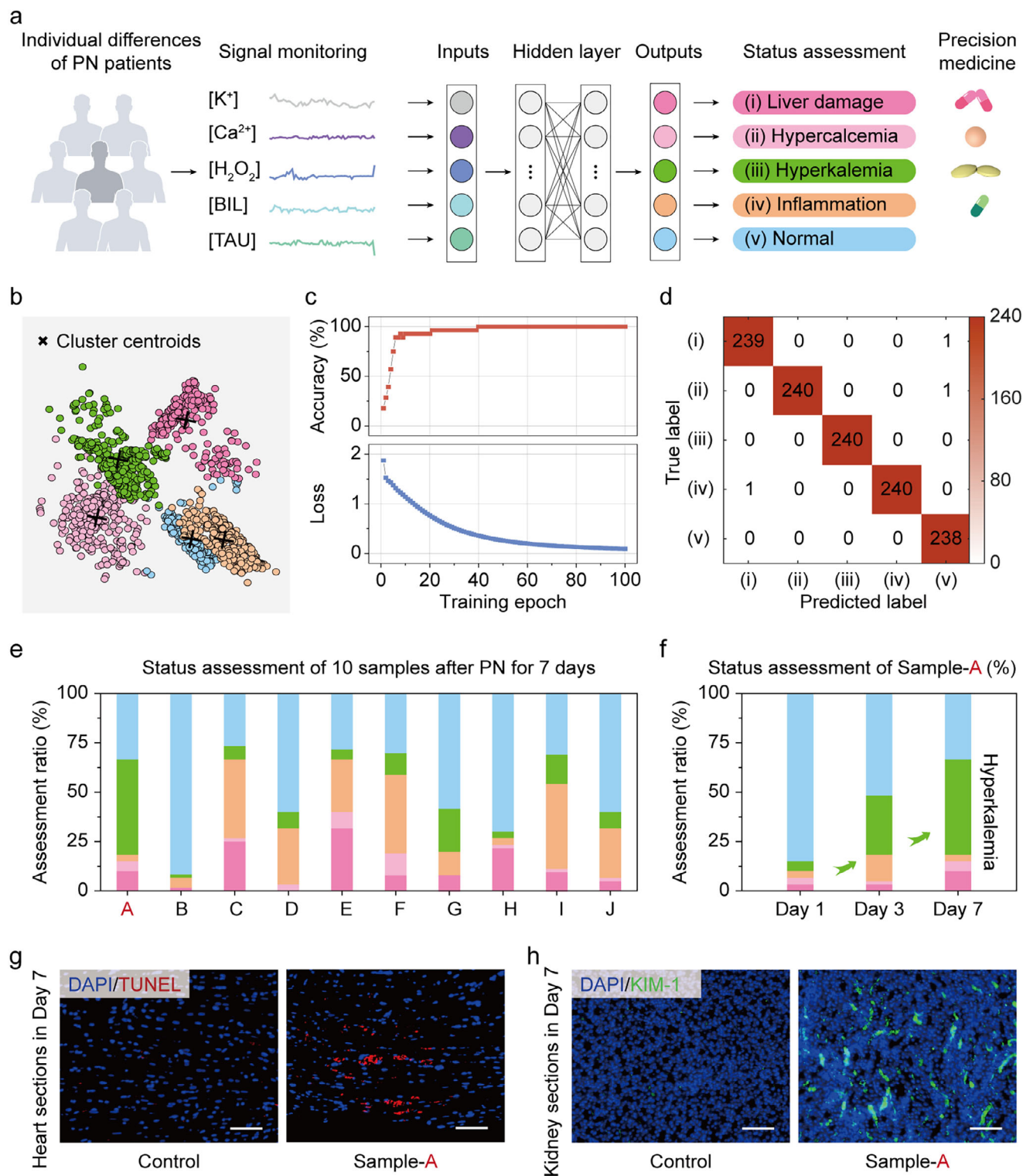


FIGURE 5 | Application of assessing complications of parenteral nutrition via machine learning. (a) Schematic illustration of signal monitoring from different individuals, status assessment by machine learning, and personalized treatment for precision medicine. (b) K-means cluster analysis of the dataset of parenteral nutrition rats in different physiological states. (c) The accuracy and loss changes of the BP neural network in 100 training epochs. (d) Confusion matrix showing the classification accuracy for distinguishing different complications in the training set. (e) Assessment ratio of various complications in 10 SD rats after 7 days of standard parenteral nutrition. (f) Assessment ratio of various complications in sample-A after 1, 3, and 7 days of standard parenteral nutrition. (g) Immunofluorescence staining for DAPI (blue) and TUNEL (red) in the heart of sample A under parenteral nutrition and control group on Day 7. Scale bar, 100 μ m. (h) Immunofluorescence staining for DAPI (blue) and KIM-1 (green) in the kidney of sample A under parenteral nutrition and control group on Day 7. Scale bar, 100 μ m.

The modular architecture of our sensing platform enables expansion beyond chemotherapy and parenteral nutrition to encompass comprehensive disease surveillance by developing an expanded biomarker sensing library. In critical care, continuous monitoring of pH, oxygen, and carbon dioxide could facilitate the early detection of respiratory failure and metabolic acidosis. For perioperative and intensive care management, real-time tracking of lactate and electrolytes could indicate tissue hypoperfusion and metabolic stress. These capabilities could extend to sepsis surveillance, cardiovascular monitoring, and multi-organ dysfunction assessment, where dynamic biochemical signatures often precede clinical manifestations. Through this plug-and-play sensing framework, our catheter system can evolve into a versatile monitoring platform applicable to a wide spectrum of clinical scenarios.

From a translational perspective, hemodynamic parameters such as venous blood flow velocity, shear stress, and Reynolds number differ between humans and rats, with the blood flow velocity in the human jugular vein being approximately 4 times that in rats. We experimentally validated the sensing performance across a wide range of flow velocities, and stable sensor responses were maintained, indicating future translational potential. Three-month implantation, as demonstrated by histology, Doppler, and hematology, demonstrated minimal inflammation, no thrombosis, and good hemocompatibility. Future clinical translation will require further validation in clinically relevant large-animal models, followed by regulatory preclinical evaluation and phased clinical trials to systematically assess device performance under human-scale hemodynamic, thrombogenic and immune environments, as well as long-term in vivo operation. In parallel, further optimization of the regeneration efficiency and antifouling performance of the DMIP layer could shorten recovery time and support longer-term, higher-frequency continuous monitoring. Collectively, this sensing catheter holds the potential to establish a new paradigm for intravascular health monitoring by overcoming the need for intermittent blood testing and providing patients with continuously updated digital reports.

Looking forward, personalized sensor configurations tailored to individual pathophysiological profiles will enable continuous monitoring across both hospital and home settings. Integration with intelligent drug delivery systems could establish closed-loop therapeutic control, while secure, real-time data transmission would facilitate the dynamic optimization of treatment regimens, from drug selection to dosing schedules. This responsive paradigm maximizes therapeutic efficacy while minimizing adverse events. Critically, the economic accessibility of our technology positions it for widespread clinical adoption and global health applications. As healthcare systems worldwide face mounting pressures from chronic disease burden and aging populations, technologies that bridge institutional and home care while maintaining clinical-grade monitoring become essential for realizing the vision of sustainable, patient-centered precision medicine.

4 | Experimental Section

4.1 | Statistical Analysis

All of the quantitative data in this research were expressed as mean $\pm$ standard error for $n = 3$ samples. All statistical analyses

were performed on Origin 2021. The analysis was performed for statistical comparisons among multiple groups. The significance of the difference was determined by one-way ANOVA followed by Tukey's post hoc test. $*P \leq 0.05$, $**P \leq 0.01$, and $***P \leq 0.001$ were considered to be significantly different and ns show no significance.

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Conflicts of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting File: adma74221-sup-0001-SuppMat.docx.