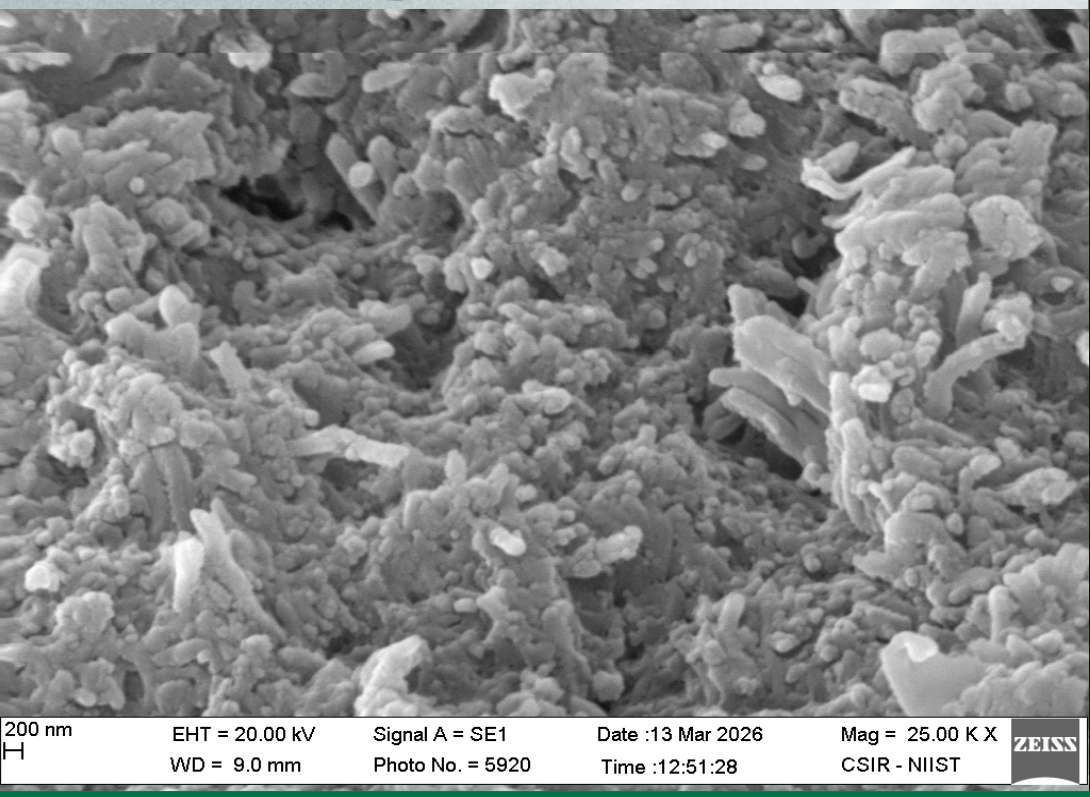


OMSTH

OPINIONS IN Medical Sciences, Technology and Health

- Flow Measurement Approaches
- High Risk Cardiovascular Devices
- Chemical Characterizations of Medical Devices

December 2025

Volume 3 Issue 2

OMSTH

OPINIONS IN Medical Sciences, Technology and Health

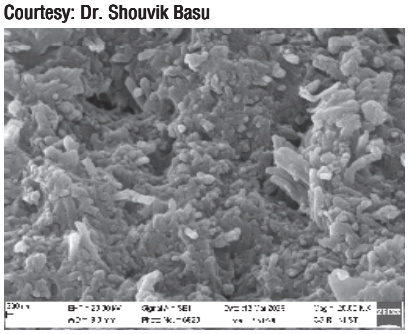
Scope

Technology has been breaking boundaries in medical sciences. We here at SCTIMST were the torchbearers of innovations in medical sciences in India by the amalgamation with engineering, basic science and public health and were responsible for the development of the first indigenous aortic valve in India. The Chitra blood bag is another success story. At this juncture, as we complete 44 years of dedicated innovations to society, the knowledge and expertise we possess on the development, validation, clinical trials, translation and commercialization of medical devices, and at the same time delivering high-end medical care in neurological and cardiological disciplines and public health, we think it is time to share and hence this Journal.

The Journal will publish reviews in the field of medical sciences with a focus on cardiological and neurological sciences, biomedical technologies, its translation and commercialisation and public health.

Cover Photo

Courtesy: Dr. Shouvik Basu



Clots play an important role in health & therapeutics. The field shows a dense, three-dimensional fibrin matrix with an irregular, highly textured surface composed of compacted fibrillar material and heterogeneous aggregates. Numerous micron-scale protrusions and lamellar/frond-like structures emerge from the main clot body, consistent with dehydrated and collapsed fibrin bundles formed during freeze-drying.

Interspersed between the denser regions are voids and pores of variable size, indicating a nonuniform porosity within the network. The overall morphology is consistent with a mechanically consolidated fibrin scaffold in which dehydration accentuates surface roughness, promotes apparent thickening/merging of fibers, and enhances the visibility of particulate deposits adherent to the fibrin framework. The scanning electron micrograph depicts the ultrastructure of a lyophilized fibrin clot imaged using a Zeiss SEM.

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OMSTH

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EDITORIAL

Three Years of OMSTH: Reflections and Highlights

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We are completing our third year of OMSTH publication. Over this period, our aim in advancing knowledge and sharing key insights in medical device development and safety has remained unwavering.

This issue presents articles that focus on the challenges in the development and manufacturing of medical devices. By examining the issues addressed here, we aim to advance a better understanding of the field and promote best practices among professionals.

Tutorial: Chemical Characterisation of Medical Devices and its Role in Toxicological Risk Assessment

One of our highlighted tutorials explores the process of chemical characterization in medical devices. This tutorial emphasizes its key role in toxicological risk assessment. Carrying out a comprehensive risk assessment, implementing in-depth risk mitigation approaches, and performing rigorous testing are all essential steps to ensure the safety of medical devices for end users, including patients, doctors, nurses, and caregivers.

Chemical characterization is the basis for the determination of a medical device's or biomaterial's biocompatibility. It involves identifying and quantifying the chemicals that could potentially be released from a device during clinical use. The primary goal of this process is to support toxicological risk assessment (TRA) by determining if patient exposure to these substances may cause harm.

Chemical characterization provides a scientific basis for biological safety evaluation, helps reduce unnecessary animal testing, detects potentially hazardous substances right in the beginning, and supports material selection and design changes. This is important as biocompatibility evaluations have shifted from the philosophy of risk evaluations to risk assessment and mitigation. This ensures regulatory compliance and enables a patient-exposure-based assessment rather than relying solely on hazard identification.

In contemporary practice, chemical characterization is commonly the primary step in determining which biological tests are genuinely necessary. The article includes a comprehensive review of this important topic.

Review: Flow Measurement in CSF Management Devices

This review examines the techniques used to measure flow in cerebrospinal fluid (CSF) management devices. For implantable CSF management devices, the most promising technologies include:

- Thermal MEMS flow sensors

Citation: A.M. Nandkumar, Editorial, Opn. Med. Sci. Technol. Health, 2025; 3(2): e25008.

Keywords: *device approval, biocompatible materials, product surveillance, postmarketing, cerebrospinal fluid shunts, equipment failure*

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- Pressure-based flow estimation
- MEMS mechanical/capacitive sensors

For external drainage systems, practical options are:

- Volumetric/gravimetric measurement
- Pressure monitoring with flow estimation

The bottom line is that there is no perfect method for measuring CSF flow. The best choice depends on the device design and its specified application.

Review: Recall of High-Risk Cardiovascular Devices

The review of the recall of high-risk cardiovascular devices discusses the circumstances under which such devices are recalled, the reasons for these recalls, and their impact on patients and caregivers. Recalls of implanted medical devices are situations manufacturers endeavor to avoid, making the process of designing and developing implantable devices lengthy and challenging.

Implantable cardioverter-defibrillators (ICDs) and pacemakers are among the most frequently recalled devices. This is because of their widespread use and the complexity of their electronic components. Despite advances in technology, battery and lead failures continue to be common, and there is a growing trend of software-related recalls, indicating the increasing application of digital technologies in medical devices.

While many recalls do not immediately result in adverse clinical outcomes, failures in high-risk devices can have grave consequences. Post-market data collection is key for identifying rare but serious device failures. Recalls of high-risk cardiovascular devices underline the balance that must be maintained between rapid technological innovation and long-term safety. Although most devices offer significant clinical benefits, failures—especially in life-sustaining devices—can have severe consequences. Therefore, strengthening surveillance, improving device design, and strengthening transparency are essential to minimize risks and improve medical outcomes.

Please read, review, and send your comments to the Editor.

REVIEW ARTICLE

Chemical Characterization of Medical Devices and Its Significance in Toxicological Risk Assessment

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Abstract

Chemical characterization of medical devices and their constituent materials is an essential step in their biological evaluation. As per ISO 10993-18, the chemical characterization provides comprehensive information about the configuration and chemical composition of a medical device, which is essential for the toxicological risk assessment (TRA). Additionally, the chemical characterization enables the establishment of the equivalence between the device under evaluation and an existing device in the market. This would support regulatory decision-making and significantly reduce the extent of animal testing required. Extractable and leachable analyses of medical devices contribute further to the TRA by providing a comprehensive understanding of chemical release from the medical device during its intended clinical use. This article aims to present an overview of the principles of chemical characterization as per ISO 10993-18, along with the crucial steps involved in the process.

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Introduction

Medical devices play a crucial role in modern medicine by facilitating the treatment, prevention, diagnosis, and management of diverse diseases. It is reasonable to state that individuals encounter one or two medical devices in their daily lives. According to World Health Organisation (WHO), a medical device refers to any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material, or other similar or related article, intended by the manufacturer to be used, alone or in combination, for a medical purpose [1].

Medical devices can be classified into different categories based on the level of risk associated with their usage [2]. The United States Food and Drug Administration (FDA) classifies medical devices into three categories: Class I (low risk), Class II (moderate risk), and Class III (high risk). In India, the Central Drugs Standard Control Organization (CDSCO) categorizes medical devices into four classes, namely, Class A (low risk), Class B (low-moderate risk, Class C (moderate-high risk), and Class D (high risk) [3].

In addition to risk-based classification, medical devices are categorized according to the duration of patient contact. Devices with patient contact of less than 24 hours are considered limited-contact devices, whereas those with patient contact

ranging from 24 hours to 30 days are classified as prolonged contact devices. If the clinical usage of medical devices exceeds 30 days, they are regarded as long-term contact devices.

Further, medical devices may be classified based on their origin or base material, such as polymeric, metallic, and ceramic medical devices. They may also be classified by mode of use, including extracorporeal (temporary external support) and implant (permanent or semi-permanent incorporation inside the body) medical devices. With the swift advancements in science and technology across diverse domains, the medical device sector too has evolved significantly, showcasing these technological innovations.

The increasing health awareness along with deteriorating living conditions, has led to a substantial growth in global medical device demand. As per recent estimates, the global medical device market was valued at approximately USD 572.31 billion in 2025, and is projected to grow at a compound annual growth rate (CAGR) of 6.90 % to reach USD 1032.66 billion by 2034 [4]. In alignment with this global trend, the Indian medical device market has also displayed significant growth and is expected to grow from USD 16.97 billion in 2025 to USD 26.66 billion by 2031 at a CAGR of 7.82 % [5].

Achieving the forecasted growth requires establishing a strong, focused research and development (R&D) infrastructure to design and develop new-generation medical technologies, and adequate facilities to evaluate their performance, safety, and functional robustness. In pursuit of self-reliance in the medical device sector, the Government of India introduced the National Medical Devices Policy in 2023 [6]. The primary objective of this policy is to establish a comprehensive R&D ecosystem capable of supporting the indigenous development and manufacturing of high-quality medical devices that are affordable and accessible to the Indian population.

Medical device development is a complex multidisciplinary process involving sequential stages that require the coordinated efforts of skilled professionals from diverse scientific and engineering backgrounds. Starting with the hypothesis, the development pathway typically includes prototype fabrication, functional performance evaluation, *in vitro* testing, preclinical evaluation and clinical evaluation. The progression is extended further to regulatory assessment, which may involve multiple rounds of review and modification before the device ultimately reaches the stage of commercialization. Even after market introduction, post-market surveillance and performance evaluation are essential for identifying potential improvements and ensuring continued safety and efficacy.

Throughout this comprehensive development cycle, medical devices undergo rigorous evaluations to establish their biocompatibility and safety. Traditionally, animal studies have been a significant component of the biological evaluation process. It is estimated that approximately 110 million animals are used annually worldwide for the testing of pharmaceuticals, cosmetics, and medical devices. Growing ethical concerns and sustained advocacy by animal welfare organizations and non-governmental agencies have strengthened the resistance to animal testing over the past several decades. Consequently, the global research community is actively exploring alternative assessment strategies that can reliably evaluate the safety of medical devices while minimizing or replacing the animal usage.

ISO 10993-18: Chemical Characterization of Medical Devices

ISO 10993 is a series of international standards that outline guidelines for the bio-

logical evaluation of medical devices, associated methods, and acceptable approaches for assessing biocompatibility. The series comprises multiple parts, currently ranging from Part 1 to Part 33, each addressing specific aspects of the biological evaluation of medical devices. Among these, ISO 10993-18 focuses specifically on the chemical characterization of medical devices and outlines how such characterization can support TRA [7]. This article presents an overview of the salient features of ISO 10993-18 and describes its significant role in the biological evaluation for the TRA of medical devices. In addition, it highlights the contribution of this standard to the reduction of animal use in medical device testing by enabling risk-based and science-driven assessment strategies.

To assess toxicological risk by chemical characterization, the data may be obtained either from information supplied by manufacturers or generated through appropriate analytical techniques. When the data provided by the manufacturer of medical device components or biomaterials is insufficient, it may be supplemented with results obtained using validated analytical methods. ISO 10993-18 outlines in detail the sequential steps involved in chemical characterization, the recommended methodologies, and the anticipated outcomes, along with the toxicological risk-related inferences that can be derived at each stage of the process [8].

Furthermore, the standard facilitates the establishment of equivalence between a new or reprocessed medical device and an already marketed device. It also enables the qualification or exclusion of novel biomaterials intended for medical device development by comparing their chemical characteristics with those of the established biomaterials. In addition, chemical characterization can be used to verify whether the final medical device faithfully reproduces the functional attributes of the predicate devices in the market and exhibits a comparable risk profile.

The equivalence of materials or medical devices can be defined and demonstrated through multiple criteria. If two biomaterials have identical chemical composition, they may be considered chemically equivalent. Similarly, if two medical devices comprise identical chemical constituents, developed by identical manufacturing and processing methods, and subjected to identical sterilization/decontamination routes, then they may be considered as chemically equivalent. Likewise, medical devices having identical component configurations, surface morphology, topography, and tribological properties may be regarded as physically equivalent.

Two medical devices are considered to exhibit material equivalence when their chemical and physical equivalence is established. Furthermore, if two medical devices share the identical intended clinical use and exhibit comparable biological endpoints, they are considered to have contact equivalence. Biological equivalence of two devices is established when they display both material equivalence and contact equivalence. These relationships are illustrated in figure 1.

Chemical characterization in accordance with ISO 10993-18 enables the identification and quantification of the constituents of a medical device and possible extractables and leachables from the device, thereby supporting the establishment of equivalence with an existing, clinically used device and facilitating TRA [9]. As outlined in this standard, chemical characterization involves a series of structural steps, which are discussed in detail in the following sections. A flow chart displaying various steps involved in the chemical characterization of a medical device is given in figure 2.

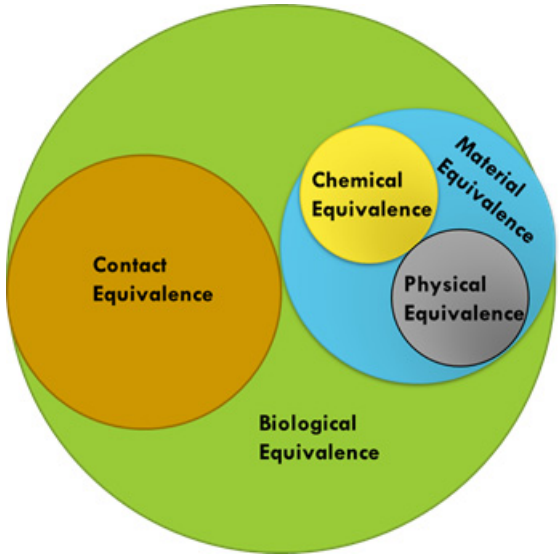

Figure 1: Equivalence concepts in medical device evaluation

Configuration of medical devices

The primary step in chemical characterization involves determining the configuration of the medical device, which involves identifying all components used in its manufacture. A medical device may be made of materials of the same type or a combination of different material classes. For instance, an insulin syringe - one of the most commonly used medical devices – typically consists of a needle, needle hub, barrel, plunger, rubber septum, and associated packaging. Device configuration analysis establishes the material class (polymeric, metallic, or ceramic) of each individual component, as illustrated in figure 3.

An array of spectroscopic techniques may be employed for component identification depending on the material type. Polymeric components can be characterized using spectroscopic methods such as Fourier-transform infrared (FTIR) spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, and Raman spectroscopy. In contrast, metallic or ceramic components may be identified using X-ray-based techniques, including X-ray fluorescence (XRF), X-ray diffraction (XRD), or atomic absorption spectroscopy (AAS). Apart from material identification, the de-

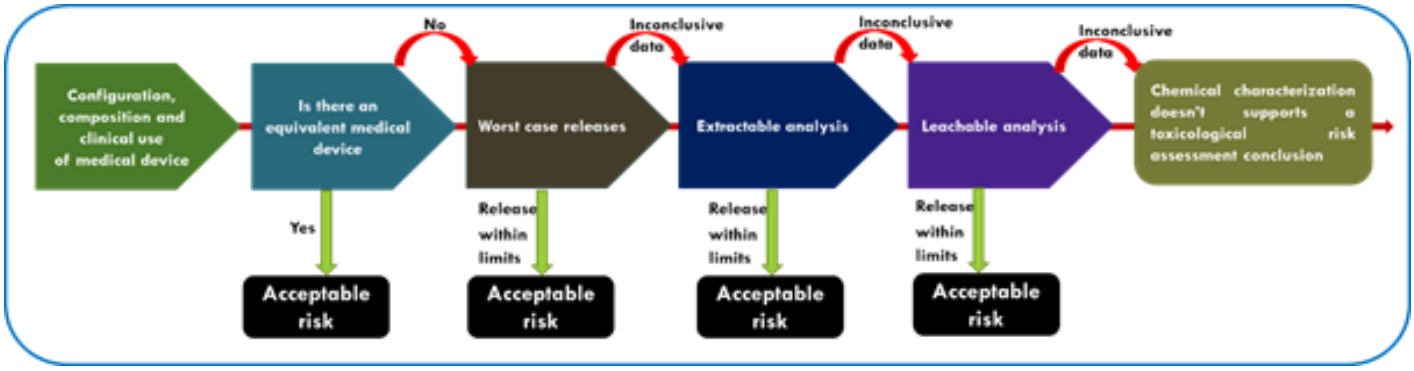

Figure 2: Flow chart showing the various steps involved in the chemical characterization of medical devices

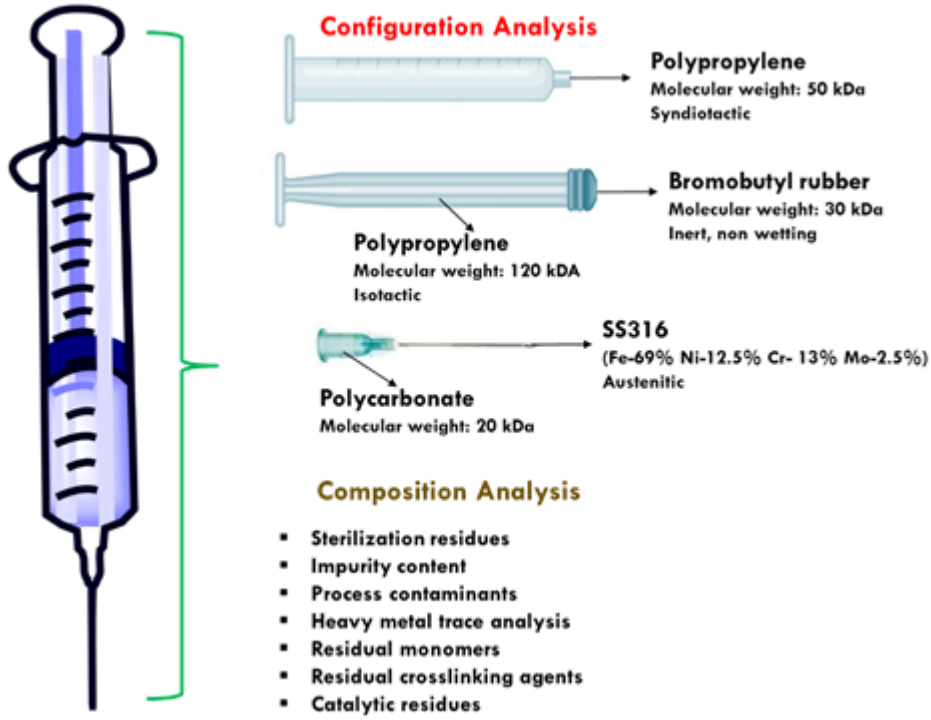

Figure 3: Configuration and composition analysis of a syringe

termination of key physical properties such as degree of unsaturation, surface composition, crosslinking density, crystallinity, molecular weight, and molecular spatial orientation (tacticity) forms an essential part of configuration assessment. These properties can be estimated using appropriate physicochemical analytical tools, as outlined in ISO 10993-18.

The concept of configuration analysis can be further illustrated using a mechanical heart valve as an example [10]. Mechanical heart valve typically comprises three integral components: an alloy frame, a polymeric tilting disc, and a polymeric sewing ring. Configuration analysis of this device would enable identification of the specific polymers and alloys used in each component, along with their key physicochemical characteristics, thereby providing a comprehensive understanding of the device composition.

Composition of medical devices

In many of the polymeric medical devices, polymers are not used in their native form. There would be functional additives that enhance specific material characteristics to meet intended application requirements. However, these additives may pose toxicological risks when present above certain threshold levels of concentrations. For instance, di(2-ethylhexyl) phthalate (DEHP) has been widely used as a plasticizer in poly(vinyl chloride) (PVC)-based medical devices to impart flexibility. The carcinogenic potential and significant reproductive toxicity of DEHP is well documented in literature [11]. Hence the detection and quantification of potential polymer additives is inevitable for the TRA.

Composition analysis of a medical device involves the assessment of the purity

of each constituent component, along with quantitative determination of impurities, catalysts, additives, residual monomers, reagents, solvents, and other processing-related chemicals present in the device. This analysis also includes the evaluation of sterilization residues, such as ethylene oxide, and manufacturing process residues, including mould-releasing agents and cleaning agents. A range of spectroscopic and chromatographic techniques can be employed to achieve comprehensive compositional characterization of medical devices. Hence, composition analysis of a mechanical heart valve enables quantitative estimation of additives, residual monomers, sterilization bi-products, and process-related contaminants present in the polymeric components, as well as the determination of hazardous elemental impurities - such as Arsenic, Lead, Cadmium, Mercury, hexavalent Chromium - within the polymers and metallic alloys used.

Following configuration and composition analyses, the analyst obtains definitive identification of the materials used in each medical device component, along with precise quantitative estimates of impurities, additives, residual monomers, sterilization by-products, and other extractable or residual substances present. This information, when considered in conjunction with the intended clinical use of the medical device, enables the establishment of equivalence with an existing, clinically proven medical device. When the configuration, material composition, sterilization method, and intended clinical application of the device under evaluation are identical to those of a predicate device, the two devices may be considered biologically equivalent. As per ISO 10993-1, if chemical characterization demonstrates biological equivalence to an existing device, no additional biological testing is required, and the device is considered to have an acceptable toxicological risk. Conversely, when configuration and composition analyses failed to establish equivalence with a predicate device, a worst-case release scenario must be considered to evaluate the potential toxicological risk associated with the device.

Worst-case release of medical devices

Worst-case release represents a hypothetical exposure scenario in which the entire quantity of chemical constituents associated with a medical device, including base materials, additives, fillers, residual monomers, impurities, processing aids, and sterilization residues are presumed to be released to the patient during clinical use. This assumption is consistent with the principle of TRA outlined in ISO 10993-17, which supports the use of protective exposure scenarios when compound-specific release data are unavailable. According to ISO 10993-17, the toxicological risk assessor shall estimate patient exposure by considering the number of devices used, device dimensions or mass, and the type, frequency, and duration of body contact, device configuration, and material composition [12]. The estimated exposure for each identified chemical constituent is then compared against established toxicological reference values, such as permitted daily exposure (PDE), tolerable daily intake (TDI), or tolerable intake (TI), as and when applicable.

If the estimated chemical exposure under the worst-case release scenario does not exceed the established toxicological threshold values, the medical device is considered to present an acceptable toxicological risk, and no further chemical characterization is required at this stage. However, when the worst-case assumptions fail to provide sufficient confidence to conclude the risk assessment due to uncertainty in the exposure estimate or proximity to toxicological thresholds, the standard suggests further refined evaluations. In such cases, chemical characterization must continue to the next stage, extractable analysis to generate com-

pound-specific release data for improved exposure and risk estimation.

Extractable analysis of medical devices

The term "*extractables*" refers to the chemical constituents that are released from a medical device or its constituent materials when subjected to controlled laboratory extraction conditions using a specified extraction medium, temperature, and duration. In an extractable analysis, the medical device under evaluation, or a representative portion, is immersed in a selected extraction vehicle under defined pH and temperature conditions for a predetermined period of time, in line with standardized protocols.

Upon completion of the extraction, the resulting extract is analyzed using appropriate qualitative and quantitative analytical techniques to identify and quantify the chemical substances released during incubation. Extractable analyses are inherently complex, as the nature and quantity of chemicals detected are strongly influenced by multiple experimental parameters, including the choice of extraction method, nature and polarity of extraction vehicle, extraction temperature, and extraction duration [13]. Consequently, careful selection and justification of extraction conditions are essential to ensure that the study provides an accurate and scientifically meaningful characterization of potential chemical exposure. The principal factors influencing the outcome of extractable studies are outlined below.

a. Extraction methods: Several extraction methodologies have been reported for the chemical characterization of medical devices, including conventional liquid extraction, Soxhlet extraction, reflux extraction, and dissolution followed by reprecipitation. Soxhlet extraction of a vascular graft is shown in figure 4. Extraction studies may be conducted using several approaches, namely simulated, exaggerated, and exhaustive extraction, depending on the intended clinical use and duration of patient contact of the device [14].

Simulated extraction is designed to replicate the actual clinical use conditions of the medical device as closely as possible and, therefore recommended for de-

Figure 4: Soxhlet extraction of vascular graft

vices with limited or short-term patient contact. Exaggerated extraction is generally considered an accelerated extraction approach, in which extraction is performed under more severe time and/or temperature conditions than those encountered during clinical use. An exaggerated extraction approach is often employed to assess potential worst-case chemical release scenarios. Exhaustive extraction, often referred to as complete extraction, involves repeated extraction cycles until the concentration of extracted analyte is reduced to around one-tenth of the initial concentration observed. Exhaustive extraction is recommended for medical devices intended for prolonged and long-term patient contact, as it would give a comprehensive estimate of potential extractables. It is advised to perform medical device extractions using chemically stable, non-reactive containers, such as borosilicate glass vessels, with closures lined with inert materials (e.g., Polytetrafluoroethylene, PTFE) to minimize background contamination and prevent secondary interactions during the extraction process.

The extraction conditions should be selected such that they do not induce chemical or physical alterations to the medical device under evaluation. If the extraction process results in apparent changes to the test article, the quantity and quality of extractable estimates may be altered, thereby compromising the relevance of the data. In cases where visible alteration of the device is observed, the resulting extract should be considered for TRA only if the alteration can be scientifically justified and demonstrated not to confound the extractables profile. Accordingly, the chemical and physical properties of the medical device materials must be carefully considered while selecting the extraction conditions.

Under exaggerated extraction conditions, extractions are commonly performed at 37 ± 1ºC for 72 ± 2 h; however, alternative time-temperature combinations have also been reported, including 50 ± 2ºC for 72 ± 2 h, 70 ± 2ºC for 24 ± 2 h, and 121 ± 2ºC for 1 ± 0.1 h, depending on the nature and characteristics of device materials, and intended clinical use of the device. For simulated extractions, the extraction temperature is typically maintained at 37 ± 1ºC for a duration corresponding to the actual clinical use period of the medical device.

According to ISO 10993-18, all extraction conditions, including extraction medium, temperature, duration, and surface-to-volume ratio, should be clearly documented and reported together with the extractables profile and quantitative estimates to ensure transparency, reproducibility, and appropriate interpretation of the results.

b. Sample: The selection of test samples for extraction has a significant role in the outcome and interpretability of extractable analysis. Wherever feasible, the entire medical device should be used for extraction to ensure a comprehensive estimation of potential chemical release. However, when the medical device is large, or when only specific components are intended to contact the patient during clinical use, representative portions of the device may be selected for extraction. In such cases, the selected samples must be scientifically justified and representative of the materials and configurations relevant to patient exposure.

For medical devices composed of multiple material types, the representative test article should include all constituent materials in proportions equivalent to those present in the final device. In addition, the material interfaces and joints should be included in the test sample, as interfacial regions may exhibit extractables profiles that differ from those of the individual bulk materials. An adequate quantity of sample should be used to ensure sufficient analytical sensitivity and to minimize the risk of failing to detect extractable compounds.

In accordance with ISO 10993-18, extraction surface area-to-volume or mass-

to-volume ratios should be selected based on the physical form of the test article. Thin films, sheets, or tubing should be extracted using a surface area-to-volume ratio of 6 cm^2/mL. Molded solid devices with thicknesses greater than 1 mm should be extracted at a ratio of 3 cm^2/mL, while elastomeric closures with thickness exceeding 1 mm may be extracted at a ratio of 1.25 cm^2/mL. For irregularly shaped solid devices, a mass-to-volume ratio of at least 0.2 g/mL should be employed to ensure adequate detection of extractable substances. In the case of irregularly shaped porous materials, such as membranes or textiles, a mass-to-volume ratio of 0.1 g/mL is generally sufficient.

c. Extraction vehicle: The selection of an appropriate extraction vehicle is determined by the objective of the extraction study. For simulated extraction, the extraction vehicle should closely replicate the physicochemical characteristics of the medium to which the medical device is exposed during actual clinical usage. In contrast, exhaustive and exaggerated extractions may employ vehicles with more aggressive solvating properties than those used for simulated conditions in order to provide a conservative assessment of potential chemical release.

Medical devices with limited or indirect patient contact may be extracted using a single simulated extraction vehicle, whereas devices intended for prolonged or long-term contact, including implant devices, should be extracted using at least two extraction vehicles of different polarities, as recommended in ISO 10993-18 and ISO 10993-12. In all cases, the choice of extraction vehicles must be scientifically justified and documented in line with the relevant standards.

Extraction vehicles should be selected judiciously, as certain materials may undergo swelling, shrinkage, or chemical degradation when exposed to specific solvents. Excessive swelling can compromise the accuracy of extractables quantification, while shrinkage or degradation may change the extractables profile. When swelling of the test material is observed, quantitative calculations should be based on the final volume of the extraction vehicle rather than the initial volume. Similarly, any changes in the extraction vehicle volume arising from evaporation or chemical reactivity particularly when volatile solvents are used should be monitored and accounted for during data analysis. Compensation for solvent loss by the addition of fresh extraction vehicle is not recommended, as this may dilute extracted constituents and confound the quantitative estimates.

To minimize solvent loss, extractions should be performed under controlled conditions that limit evaporation. Regardless of the underlying cause, reductions in extraction vehicle volume during extraction must be recorded, and the exact final volume of the extraction vehicle should be reported alongside the analytical results to ensure transparency, accuracy, and regulatory acceptability of the extractables assessment.

For the estimation of residual monomer content, filler content, plasticizer content, etc., the polymeric medical device specimen may need to be dissolved in suitable solvents and precipitated by the addition of specific anti-solvents. Each polymer has specific solvents and anti-solvents, which need to be selected judiciously to harness the required quantitative information. The list of solvents and anti-solvents for common polymers is mentioned in ISO 10993-18.

Sometimes, the biological testing can be correlated with chemical analysis. Mostly, the solvents used in both tests are comparable and have similar properties. But in some cases, the solvents used for biological testing may not be suitable for chemical analysis. In such cases, a surrogate extraction vehicle suitable for chemical analysis should be used. The extraction of biological test media with a chemically analyzable extraction vehicle is another approach. For example, a 1:1 v/

v mixture of ethanol and water can be used as a surrogate extraction vehicle to replace vegetable oil used in biological testing. Similarly, volumetric mixtures of ethanol and saline can be used as surrogate extraction vehicles to replace culture medium with serum (2:3 ethanol and saline) and without serum (1:9 ethanol and saline).

The extract of the medical device obtained by different extraction protocols will be analyzed using various screening and targeted techniques to get detailed information about the extractables. Mostly chromatographic techniques are employed for the extractable analysis [15,16]. There will be volatile, semi-volatile, and non-volatile organic components in the extract along with elemental and ionic residues. Volatile and semi-volatile components can be estimated using gas chromatographs with various detectors, whereas non-volatile components are often estimated with liquid chromatographic tools. Inductively coupled plasma (ICP) spectrometers can be employed for the trace-level detection of elemental components in the extract, whereas ions released into the extract from medical devices can be estimated using ion chromatographic techniques.

Highly sensitive mass spectrometers coupled with a liquid chromatograph or a gas chromatograph are employed for the non-targeted screening of components in the medical device extract. As they are highly sensitive, there will be innumerable peaks in the chromatogram obtained for a simple medical device extract. Among these peaks, the selection and omission of peaks for TRA is governed by an analytical evaluation threshold (AET). AET is a concentration-based threshold value, much like the dose-based threshold toxicological concern often employed in a clinical setup [17]. AET depends on the number of devices used for preparing the extract (A), the volume of extraction vehicle used (B), clinical exposure of the device (C; number of devices used per day per patient), dose-based threshold

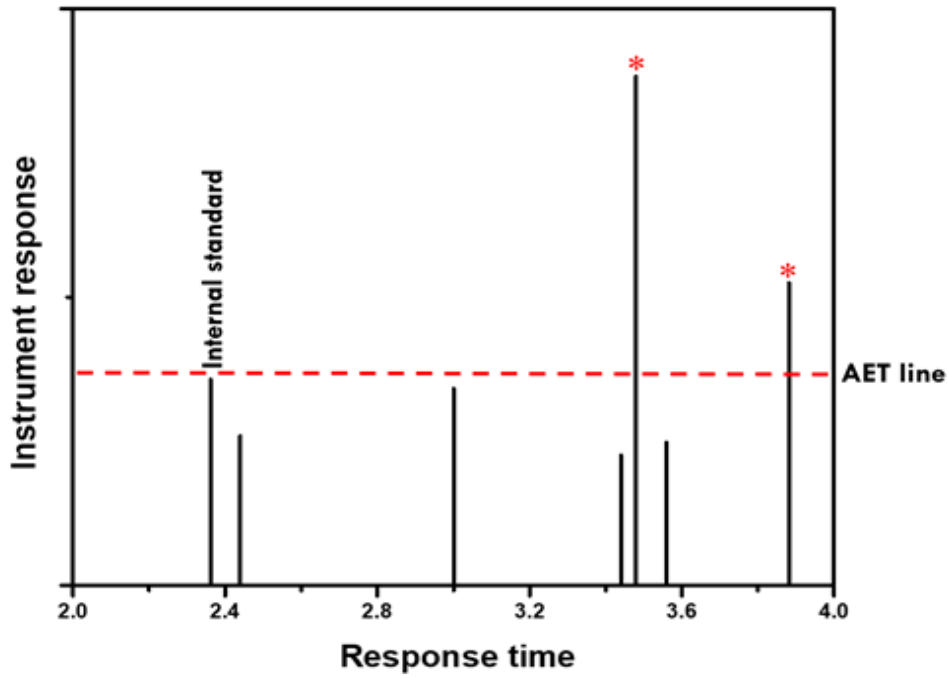

Figure 5: Relevance of AET in screening the extractables. Peaks marked with an asterisk above the AET line are to be identified and quantified

(DBT), and the uncertainty factor (U) of the analytical method used for extract analysis. AET calculated using the equation given below:

$$AET = \frac{DBT \times \left(\frac{A}{B \times C}\right)}{U}$$

Consider 10 ng/ml is the AET calculated for a medical device under consideration. During the non-targeted analysis of the extract, those peaks present below the threshold line of 10 ng/ml can be omitted unless they correspond to one of the cohorts of concern (CoC). CoC is a group of extremely potent toxic components, such as organophosphorus compounds, heavy metals, polycyclic amines, steroids, azo compounds, dioxins, aflatoxin-like compounds, etc. [18]. All peaks above the threshold level, along with all the cohorts of concern present, should be considered for the targeted analysis and must be used for the TRA of the medical device (figure 5).

The details of the extractable analysis, including the detailed quantitative estimation of all the components above the AET, along with the details of CoC, will be scrutinized by the toxicologist. If the extractable analysis confirmed that the chemical release from the medical device under the exaggerated laboratory condition is well within the toxicological limits, the medical device can be considered to have an acceptable health risk, and the chemical characterization can be stopped. If the extractable analysis failed to give a satisfactory conclusion about the safety of the medical device, the chemical characterization needs to be continued to the next step, leachable analysis.

Leachable analysis of medical devices

Leachable analysis is more realistic than the extractable analysis. During the extractable analysis, the medical device is subjected to harsh laboratory conditions to extract all the chemical components likely to be released from the medical device. In contrary, leachable analysis employs milder conditions exactly mimicking the physiological conditions in which the medical device is actually used. The commonly used vehicles for leachable analysis include phosphate buffer saline, ethanol: water mixture, buffers, etc., mimicking the physiological media, and the incubation conditions will also be milder than those used for extractable analysis. After extracting the leachables, the leachate can be analyzed using the chromatographic and spectroscopic methods mentioned above for extractable analysis. Detect and quantify all the leachable components above the AET value, and the quantitative information has to be used for TRA. If the toxicologist confirms that the leachable concentrations are well within the acceptable limit, the device can be considered to have an acceptable toxicological risk, and the chemical characterization data can be used to support the biological evaluation of the medical device [19]. If the leachable analysis fails to give a satisfactory conclusion to the TRA, the chemical characterization data cannot support the biological evaluation of medical devices, and obviously, the risk analysis should be done by animal studies alone.

Thus, the chemical characterization of medical devices as per the guidelines of ISO 10993-18 provides valuable information about the chemical features of the device and device components that could be utilized for their TRA.

Conclusions

Biological evaluation of medical devices is one of the inevitable steps in the medical device development. ISO 10993-18 provides the framework and guidelines to

perform the chemical characterization of medical devices and the utilization of the data for their TRA. Configuration and composition analysis of medical devices, along with the information about patient contact, will enable the analyst to establish the equivalence of a medical device with another one already in the market. If the chemical characterization supports the biological equivalence of the medical device under consideration with an established medical device, it can be considered to have an acceptable risk. If the composition and configuration analysis fails to establish equivalence, the chemical characterization has to be continued to extractable and then to leachable analysis to estimate the toxicological risk. Thus, the chemical characterization as per ISO 10993-18 supplements the biological evaluation and TRA of medical devices and thereby helps to reduce animal studies considerably.

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REVIEW ARTICLE

Flow Measurement Approaches in Cerebrospinal Fluid Management Devices

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Abstract

Hydrocephalus is defined as the abnormal accumulation of Cerebrospinal Fluid (CSF) leading to increased intracranial pressure inside the lateral ventricles of the brain. The disease is caused by several factors related to age and other cerebral conditions. The CSF shunt, as well as the external CSF drain, remains a primary treatment method. However, these devices are subject to blockage or revisions due to the CSF parameters and compositions, leading to underdrainage, overdrainage, or complete blockage. Therefore, it is important to measure the flow of CSF through the CSF drainage systems and shunts to monitor the proper functioning of the device and ensure better patient care without surgical methods using non-invasive methods. Various sensing methods, including optical, electrolytic bubble production based, ultrasonic, radioisotope based, resonant frequency based, thermal based, capacitive-based and charge-based systems, are used for flow measurement, which is captured in the paper. Various challenges related to translational readiness need to be addressed, including the bio compatibility, long-term stability, power management, electronic circuit management, integration with the shunt or drainage systems, and regulatory-related documentation. The emerging trends in flexible electronics, wireless telemetry, battery technologies, microsensors, which are energy efficient and data driven adaptive controls, benefit the next level of improvement in flow monitoring and better patient care.

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Introduction

Background on Hydrocephalus (Definition, Prevalence, Complications)

Hydrocephalus symptoms vary widely based on age and severity of the condition. In young children, symptoms include an abnormally large head circumference, rapid head growth, a bulging fontanel, pronounced scalp veins, vomiting, irritability, lethargy (excessive sleepiness), inability to feed, sunset eyes, and possibly seizures or developmental delays. In older children and adolescents, symptoms typically include headache (usually a severe headache in the morning), nausea, a tendency to vomit, vision issues (either blurred or double vision), lack of ability for movement coordination, excessive sleepiness, personality changes, memory

issues, and urinary incontinence. In adults and individuals with Normal Pressure Hydrocephalus (NPH symptoms can include headache, nausea, vision issues, recognizable imbalance and gait changes, cognitive deficits (memory, thinking delays, personality changes), and urinary incontinence. It is important to note that these symptoms can be like other diagnoses and should, therefore, be assessed by a medical professional [1].

Aim and Scope of this Review

Through this article, the aim is to provide an overall insight and a critical review of the current approaches to Cerebrospinal Fluid (CSF) flow monitoring in CSF management devices, including Hydrocephalus Shunts and External Ventricular Drains. The shunt technology has been playing a pivotal role in CSF/ Hydrocephalus management. However, the need for high revision rates, recurring challenges, and delayed detection has demanded the need for the devices to monitor the CSF through the shunt device. This review paper gives a comprehensive idea of the existing techniques on which research was conducted by various researchers in flow monitoring techniques.

The scope of work in this review paper includes:

- Historical evolution of the shunt systems and the need for device-based observation as part of clinical evaluation.
- Different monitoring strategies of the flow through the shunts.
- Challenges associated with the clinical translation of flow monitoring devices.
- Future scope of research in the field of flow monitoring devices.

The goal is to create a comprehensive framework of the different research on the flow monitoring of CSF shunts and external CSF drainage systems, which ensures an understanding of the available research and implementations in this domain. This gives a consise overvies on the available principles on the flow monitoring techniques in CSF management devices. The article summarizes the studies, reported accuracies, strengths, and limitations as reported by different authors. However, a comparison of different principles is not part of this scope.

Historical Context of Hydrocephalus Management

Frequently documented cases of hydrocephalus were recorded by Hippocrates, Galen, and Arab physicians in the early and medieval periods, which they believed resulted from an extracerebral accumulation of water. The first meticulously detailed description of a surgical intervention, specifically the evacuation of superficial intracranial fluid in pediatric hydrocephalus patients, was not recorded until the tenth century by the pioneering physician Abul Kassim Al Zahrawi. His comprehensive account represents a pivotal advancement in the historical understanding and management of this complex neurological condition. Effective hydrocephalus treatment became viable only in the late 19th century, driven by advances in aseptic surgery and pathophysiological understanding. Early progress included Wernicke's 1881 sterile ventricular puncture and external CSF drainage, Quincke's 1891 serial lumbar punctures, and Mikulicz's 1893 pioneering permanent shunt. While various shunts developed until 1925 often failed due to poor materials, a major breakthrough occurred in 1949 with Nulsen and Spitz's successful caval vein shunt. The combination of artificial valves and silicone around 1960 revolutionized global therapy, though newer adjustable valves still face economic and technical hurdles. The 1990s saw a renaissance of endoscopic ventriculostomy, now a preferred method for adult obstructive hydrocephalus. However,

both advanced valves and endoscopic ventriculostomy currently lack comprehensive long-term evaluations [2].

The cure for hydrocephalus begins with the time beginning the strategy in which the overaccumulated CSF is diverted to a different compartment inside or outside the body. The early approaches in the 19th and 20th centuries involved methodologies including ventricular punctures, which were riskier as far as infections and other mechanical failures. During that period, the external ventricular drain was introduced in the mid of 18th century, which was a temporary solution for hydrocephalus management. A major revolution occurred in the middle of the 20th century with the introduction of the Ventriculo Peritoneal (VP) shunt, which was implantable.

The initial shunt systems involved non-adjustable type valve which are with simple designs and ensuring a uni directional flow, opening at a minimum fixed opening pressure. These designs were later associated with complications including over or under-drainage, mechanical blockage, and infection. The later advancement addressing this problem was the introduction of the programmable shunt, in which the minimum opening pressure could be adjusted using an external magnetic controller. There were also advancements in which flow-regulated mechanisms [3] were introduced. Devices with anti-siphon mechanisms were also developed.

However, there was an additional problem which still remaining unaddressed after several advancements, which is crucial for monitoring the flow through the shunt. Many papers report a high revision rate of nearly 50% [4] of the implanted shunts which are mainly caused by the mechanical complications. Analysis of the flow is crucial as far as the detection of mechanical complications, including blockage or over-drainage is concerned. However, it is challenging to design a flow meter to measure flows in the range of 5 to 50 ml/hr especially since this is the nominal CSF flow rate through the shunting devices. In this context, it is important to explore different research studies available to measure CSF flow in that range. Some of the papers, including Solera et al. [6] have provided a simmilar consise overview of the available concepts of flow management devices. However, the current paper lists a more comprehensive review of all the available principles - optical, magnetic, thermal ultrasonic, radio isotope based, resonant frequency-based, capacitive based etc

Methods

A targeted literature search was performed on the different techniques identified for flow montoring of CSF management devices and based on the available data we categorised as optical, magnetic, thermal ultrasonic, radio isotope based, resonant frequency-based, capacitive based etc. The papers were identified as related to each technique. Studies only focussing on CSF management devices flow monitoring system were identified and a comprehensive overview was prepared which were finally summarized in table 1 .

Flow Measurement in Hydrocephalus Shunts: An Overview

When it comes to hydrocephalus shunts, any type of flow measurement is extremely important given the high failure rate and diagnostic conundrums that inevitably come with shunt devices. Flow measurement does provide early warning systems for shunt malfunction (e.g., under-drainage, over-drainage) and offers objectivity for shunt function while preventing severe clinical symptoms and significant ventricular changes on imaging. This measurable information assists the

decision-making process of treatment in regard to altering shunt function and optimizing CSF drainage. Improving flow measurement may reduce shunt revisions and surgeries. In addition to clinical relevance, the value of flow data is pertinent in research and development, as it may be used in creating improved shunt systems. There are current technologies for flow measurement (e.g., phase-contrast MRI (PC-MRI), a noninvasive and quantitative CSF flow measurement), and there are new technologies involving sensors working on different principles of operation.

Optical-based flow sensor

Garrett et al. [5] demonstrates a microfluidic flow sensor which is passive and biocompatible. It monitors the CSF flow without the use of implantable electronics. A thin PDMS cantilever with a reflective gold tip is placed inline with the shunt. The cantilever deflects with the CSF flow, which is detected by an external light source which is of the wavelength in the range of 620 to 625 nm produced by a LED light source of 5 W and hence, flow can be assessed non-invasively. The values in the range of 20 to 120 ml/hr are successfully measured. Two weeks of continuous flow testing are carried out. The study opens the possibility of miniaturizing and integrating the flow measurement system with the existing shunt system. Solera et al. [6] demonstrates a flow sensor, which works in the principle which relates the cantilever deflection with the applies fluid force on it. The sensor is a micromechanical cantilever fabricated from SU-8 negative photoresist, which is coated with a thin metallic layer. The sensor acts as a separate compartment of the shunt system. The flow rate is measured as a quantity that is proportionate to the deflection of the cantilever. This deflection is detected optically by the angle of reflection of the reflected infrared laser beam from the cantilever tip. The changes in flow velocity are related to this angle of reflection. The system is highly sensitive and it gives proper measurement of flow rate in the range of 20 to 90 ml/hr. There is no need for invasive readout since the detection of the laser beam is done externally. Additionally, the shunt design does not need to be altered since it is an additional enhancement.

Magnetic Tunnel Junction (MTJ) Sensors

Enikov et al. [7] proposes a Magnetic Tunnel Junction (MTJ) sensor to detect the

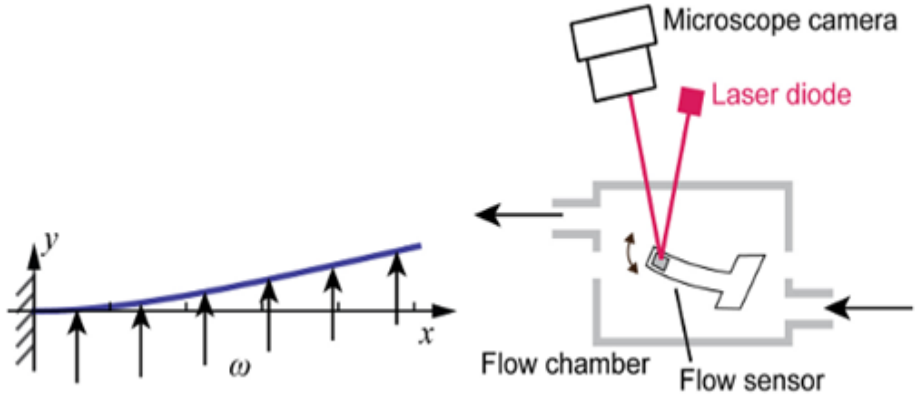

Figure 1: Optical and Cantilever based Flow sensor by Solera et al. Reproduced from Soler et al. [6] with permission

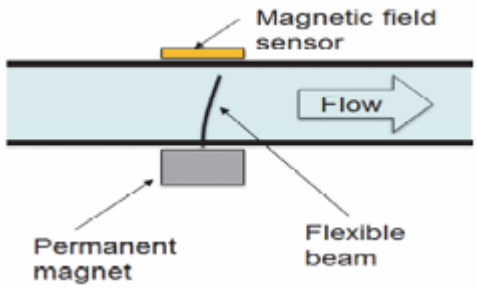

Figure 2: Flow detection principle by Enikov et al [7]. Reproduced with permission

cerebrospinal fluid (CSF) in ventricular-peritoneal (VP) shunts. A micromechanical flow sensor, in which ferromagnetic flaps bend in response to fluid movement, is incorporated into this device. The magnetic field produced is altered by the flaps while bending, which is captured by the MTJ sensor. The system also has 650 nm infrared laser source that emits the laser externally and a microscopic camera to measure the angular deflection. The sensor is optimized to achieve a 1 ml/hr resolution and a volumetric error within ± 3.2 mL over 24 hours.

Bubble Production Technique

A new implantable device has been developed by Hara et al. [8] to measure CSF flow through a Ventriculo Peritoneal Shunt (VP). The device works on the principle that the bubbles produced in the CSF drainage tube traverse at the velocity of the fluid flow. The bubble is generated by electrolytic action with the aid of an electric circuit in which a 200 kHz generator provides alternating current to a transmitting coil. The receiving unit, which is a coil, is tuned to produce 200 kHz current using a capacitor;hence, rectification is done using a silicon diode and also a Zener diode to produce a 20 V DC output. The recorder detects the bubbles in each time using two ultrasonic probes. The time difference is noted, with which velocity can be calculated.

There were different enhanced systems proposed by Numoto et al. [9] based on the principle of electrolytically generated bubbles which were detected using an impedance-based method in addition to Doppler ultrasound. There were different enhanced systems proposed by Numoto et al. [9] based on the principle of electrolytically generated bubbles, which were detected using an impedance-based method in addition to Doppler ultrasound. A tube electron complex with segments of stainless steel was embedded in silicone rubber tubing within the shunt line, where the passage of bubbles across the electrode gaps affected the electrical conductivity of the CSF column. This increased the impedance, which was measured by the noninvasive surface electrodes. This offered a superior signal to noise ratio when compared to Doppler ultrasound and better detection of flow rates less than 0.05 ml/min. There were successful animal studies of flow rates in the range of 0.01 to 0.10 ml/min and clinical studies involving 11 patients at flow ranges between 0.01 and 1.93 ml/min. The findings involving these systems monitored how the flow varies as the days progress.

Other developments include the ultrasonic transit time flow sensor developed by Pennel et al. [10] and Lam et al [11] which is a low frequency (~30 kHz) and low-amplitude (30 kPa) ultrasound.

Pennel et al. developed a system applicable for external ventricular drains,

which provided noninvasive, real-time CSF flow measurement with ±1 5% or ± 2 ml/hr accuracy, enabling early shunt obstruction detection.

The system developed by Lam et al. generates microbubbles within the shunt lumen that scatter sound waves. This allows Doppler-based measurement of flow rates as low as 3 ml/h.

Radioisotope Technique

The study done by Hidaka et al. [12] incorporates a noninvasive device with radioisotope for flow measurement. The study evaluates the CSF shunt function under different patient postures. The radioisotope, which is injected into the reservoir, is ^{99m}Tc-pertechnetate (3.7 MBq in 0.01 mL). A small detector (cadmium telluride) is provided on the reservoir of the shunt device to detect the gamma radiation emitted by the small dose of radioisotope.

The reading of the radioisotope count rapidly reduces from the supine to the sitting position of the patient. This rate of isotope clearance gives the CSF flow rate. The authors did study in four clearance patterns in which they observed almost no clearance over time in the case of Pattern 1 (no flow/obstruction) and slightly delayed clearance for Pattern 2 (adequate flow with moderate opening pressure). A little better clearance was observed for Pattern 3 (adequate flow with low opening pressure and very rapid clearance for Pattern 4 (excessive flow). The flow conditions were well matched with patients' clinical conditions.

Resonant Frequency Modulation Methods

Raj et al. [13] designed a system incorporating an external spectrometer which is wireless for the purpose of flow measurement. The pressure-sensitive capacitor of 5pF (nominal) with an air gap paired with an inductor circuit forms a resonant circuit. The resonant frequency in the range of 2000 to 400 MHz is being measured, which is matched with the CSF flow rate. There is drift of less than 0.3 ml/h observed at constant flow. The resonant frequency exhibits a second-order polynomial relationship under variable flow conditions. The flow rates were validated up to 25 ml/h.

Thermal-based flow measurement

An innovative in-line sensor was developed by Qin et al. [14] to monitor cerebrospinal fluid (CSF) flow in patients with hydrocephalus. An in-line flow sensor for hydrocephalus is a unique type of device that is designed to be installed directly into the cerebrospinal fluid (CSF) shunt system and continuously and quantitatively monitor fluid flows such as CSF drain flow rates. This sensor primarily uses thermal sensing, where one thermistor serves the function of being both a heater and a temperature sensor, and uses its heater to emit heat to produce a heat pulse using its heater, followed by detecting the change in temperature of the CSF, which allows the sensor to relate its net temperature change to the flow rate of the fluid. This real-time data allows for the timely identification of shunt failures, such as blockage or over-drainage, to provide critical real-time information to improve patient care.

The sensor consists of a single thermistor that can both heat the fluid around it and detect changes in fluid temperature. The thermistor is energized in the heating mode at a voltage pulse of 5 seconds and in the sensing mode wired to the Wheatstone bridge, in which the output is proportional to temperature. The change in output from the bridge (ÄV) before and after the heat pulse will be a function of both the CSF flow rates through the sensor and the external tempera-

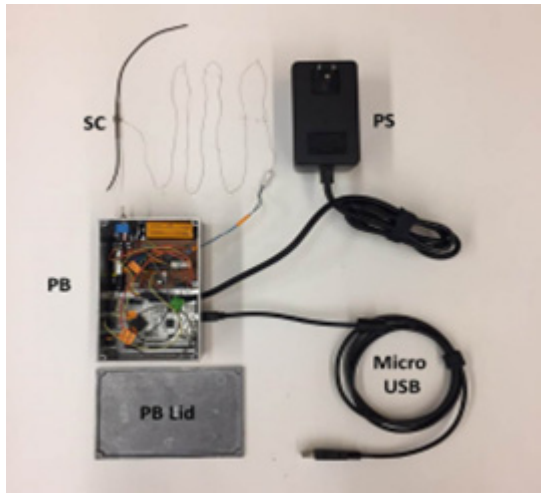

Figure 3: Inline thermalbased flow sensor system developed by Qin et al. for experimental evaluation in swine [14]. Reproduced under the Creative Commons Attribution License

ture. An empirical equation that produces flow rate estimates was developed based on in vitro and in vivo flows, with predicted flow rates having an overall RMS relative error of 6.3% for flow rates of 0 to 52.5 mL/h, at a temperature of 32 to 39 degrees. This method constitutes a replicable, quantitative means of assessing shunt function, which overcomes many challenges posed by previous methodologies that were often laborious, invasive, and required the presence of trained professionals. This sensor was purposely designed with consideration of clinical applications so that ensuring proper management and monitoring of CSF flow in patients with hydrocephalus would be much easier.

Rajasekaran et al. (2014) [15] did work on a non invasive thermal time of flight (TTOF) flow sensing and monitoring system for CSF through Hydrocephalus Shunts. In the work, silicone tubing was embedded with a titanium reservoir, which acts as a conduction interface with the cooling source, such as an ice cube. The thermal samplers situated downstream of the reservoir record the temperature,, and the delay in the recording of the cooling pulse is noted.

The ratio of the distance between the thermal samplers (Äx) to the difference in time (Ät) is noted as the flow velocity $u = {}^{\Delta x}/_{\Delta t}$. This strategy successfully worked for the flow velocities between 0.5 and 1.0 mm/s .

Qin et al. [14] developed a compact in line incorporated a thermistor-based sensor. The thermistor is a brief heater cum temperature sensor with the use of a Wheatstone bridge. This enables flow monitoring in the range of 0 - 52.5 mL/h. This sensor was able to clearly distinguish between the no-flow and normal flow conditions.

Bork et al. [17] developed a similar microfluidic sensor incorporating a thermal anemometer which is a Complementary Metal-Oxide-Semiconductor (CMOS) based having a wireless RF telemetry (13.56 MHz) which is packaged between borosilicate glass wafers which are hermetically bonded. This system successfully measures flow rates between 2 to 40 ml/hr at +/-10% accuracy.

Krishnan et al. [18] mentions about continuous, non-invasive, and wireless monitoring system for cerebrospinal fluid (CSF) flow through shunts which is a wearable, real time monitoring skin mounted flow sensor and avoids the surgical

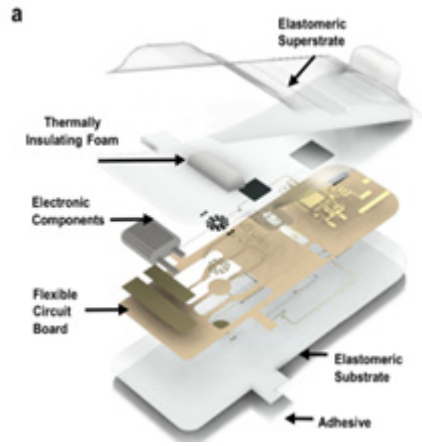

Figure 4 : Illustration of the wireless CSF flowmonitoring device developed by Krishnan et al.[18], showing the flexible circuit board, electronic components, thermal insulation foam, elastomeric encapsulation, and adhesive layers. Reproduced under the Creative Commons Attribution license

procedures and invasive testing that cause pain, discomfort, risk, and/or adverse outcomes. It also allows for continuous real-time monitoring of CSF flow, resulting in a more timely discovery of shunt malfunction. Its utility may extend further, offering the possibility for remote monitoring as well as, in turn, remote patient management, helping patients feel like they have some support outside of a clinical environment. Patients can also access and interpret the data via their mobile devices, enhancing comprehension and encouraging engagement, bringing patients and healthcare stakeholders closer together. The innovative sensors work by acting as sensors for the transport of heat through the layers of skin near the surface over the shunt. A soft, flexible, skin-conformal device, which is soft and flexible, is placed over the skin, containing thermal actuators and sensors. The device can create a localized thermal signal and measure the temperature changes that occur, reflecting the effect of CSF flow underneath the skin and its velocity. The device transmits the data wirelessly via Bluetooth Low Energy (BLE) to a mobile device or computer for further analysis.

A product that was widely used for CSF flow applications commercially, as well as mentioned by several papers [19-22] are devices by Sensiron especially SLF3S-0600F works on the principle of Thermal measurement. The SLF3S-0600F is a

Figure 5: SLF3S-0600F flow sensor Source: Sensirion [20]. Reproduced with permission

compact liquid flow sensor for bi-directional measurement up to ± 2000 µl/min, calibrated for water and IPA. It features a fast response (<20 ms), temperature compensation, and I²C digital output. Built on CMOSens® technology, it offers high reliability and integrates easily via standard fittings and mounting clamps.

Capacitive and Charge-Based Shunt Flow Measurement

The capacitive-based sensor was proposed by Chen et al. [23] for the the application of ventriculoamonioti shunt which was developed for the treatment of fetal hydrocephalus.

Chen et al. [23] proposed an integrated capacitive micro flow sensor for the application of ventriculoamniotic shunt for fetal hydrocephalus. The sensor uses a stretchable parallel plate capacitor formed from magnesium layers separated by 2 ìm dielectric elastomer and encapsulated in silicone. The deformation of the sensor produces capacitance changes in the range of 0.49–1.43 pF, which correspond to flow velocities between 0.037–0.3 m/s.

Zarrin et al. [24] proposed a compact, ultra–low-power CSF flow sensor for the flow monitoring application in Ventriculoperitoneal shunts. The sensor successfully measures flow rates in the range of 0.01 to 0.90 mL/min and consumes only ~37.5 µJ per measurement. The sensor operates by inducing a localized charge through emitter electrodes across the catheter, creating ion clouds that are carried with the flow. The downstream detector senses the voltage signal. The time delay between the charge induction and detection was measured. The ratio of the distance between the emitter and detector to the time delay is estimated as the velocity of flow.

Summary Table

The table 1 lists the summary of principle, reported flow performance, comments on accuracy, error or drift, validation level, strengths and limitations of different flow monitoring concepts reported by different authors. This table demonstrates a concise overview of the approaches that have been experimented with in CSF flow monitoring in shunts and related drainage circuits. One could compare the operational ranges, level of validation, strengths, and limitations mentioned in the paper for a quick assessment of in vivo or clinical feasibility. This information is intended to provide overall support for technology selection and future device development.

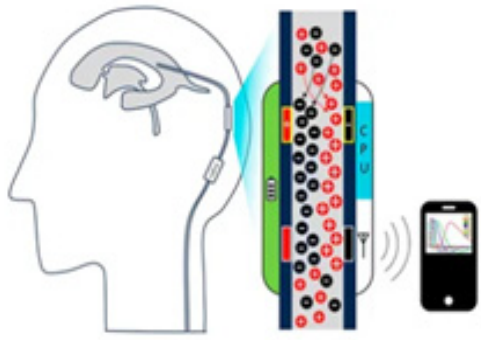

Figure 6 : Flow sensing system developed by Zarrin et al. [24]. Reproduced under Creative Commons License

Table 1: Summary table

Sensing modality / principle	Representative study (Ref.)	Comments in the study on flow performance (range / detection/ resolution)	Comments in the study on accuracy/ error/ drift	Comments in the study on validation level	Comments on Strengths as per details in the study	Comments on Limitations as per the details in the study
Optical, passive microfluidic cantilever with external optical readout	Garrett et al. [5]	20–120 mL/hr range; Linear detection; 1.9×10?³ mm/(mL/hr) sensitivity; detects pulsed & ramp flows	No drift after 2-week continuous test; stable linear	In-vitro only (artificial CSF + skin phantoms), no animal or human studies	Passive, biocompatible, non-invasive optical readout, low pressure drop, miniaturizable, stable long-term	Authors didn't do in-vivo validation; optical dependence on skin thickness; small displacement signals; artificial CSF differences
Optical micromechanical cantilever; laser reflection angle	Soler et al. [6]	20–90 mL/h	Stable, repeatable modulation was reported at 60 mL/hr. Good linearity across physiologic flow range (20–90 mL/hr)	Tested using a programmable syringe pump. No in vivo evaluation.	External readout uses biocompatible materials already common in shunt valves (PDMS, polypropylene)	Authors didn't validate the device in vivo level and other related effects. Optical alignment of the IR camera was demanded.
Magnetic flap deflection sensed by MTJ (and optical angle measurement described)	Enikov et al. [7]	CSF flow stated as pulsatile 1–100 mL/hr, resolution ~1 mL/h	Thermal sensitivity reported ~3.9 V/°C. Under zero net flow, integrated volume error over 24 h ~ - 1.8/+3.2 mL/24 h (after drift mitigation approach). Faraday cage reduced noise amplitude from ~150 mV to 50 mV.	Simulation + benchtop testing (peristaltic pump, pulsatile forward/reverse, electronics/noise tests, long-duration drift observation). Corrosion testing by cyclic voltammetry. No in vivo/clinical validation reported.	Miniaturized in-line concept; full-bridge MTJ improves SNR; shows noise shielding benefit; reports corrosion-rate estimates; dynamic response τ ~0.4s.	High temperature sensitivity/drift; earlier transducer buckling/latching; reports mainly sensitivity & drift-volume error (not full metrology like accuracy/MDF across range); no in vivo.
Bubble production by electrolysis; bubble transit measured (ultrasonic probes)	Hara et al. [8]	0.033–1.0 mL/min (animal test) 0.05–0.78 and 0.12–0.55 mL/min (24-h clinical cases)	Accuracy not stated; correlation coefficient r = 0.995 between actual and measured values.	In vivo animal validation and clinical feasibility (24-h monitoring in 2 patients)	Implantable bubble generator + external Doppler enables near-continuous/repeat monitoring,	mainly low-flow Doppler dependence and high-flow frequency response.
Electrolytically generated bubbles detected by impedance (and/or Doppler)	Numoto et al. [9]	Detection <0.05 mL/min (<3 mL/h); animal 0.01–0.10 mL/min (0.6–6 mL/h); clinical 0.01–1.93 mL/min (0.6–115.8 mL/h)	Statistically good accuracy. Reported correlation between calculated and actual flows - 0.881	Animal + clinical (11 patients)	Better SNR than Doppler (as stated)	Impedance approach requires additional implanted unit; Doppler method sensitivity limited at very low flows due to artifacts when gain is increased.
Ultrasonic transit-time flow sensing (EVD)	Pennell et al. [10]	Flow: 0.5 mL/hr (bench-stated). Clinically observed mean flows include ~10.67 mL/hr (pre-recovery) to ~0.25 mL/hr (post-recovery) in an illustrative case; waveforms show the capability to track higher pulsatile flows	±15% or ±2 mL/h 24-hr bag-weight vs. sensor volume errors: pediatric mean - 6.95 ± 3.64%; adults mean - 3.25 ± 5.96%	Observational clinical validation in humans (5 pediatric + 11 adult EVD patients)	real-time continuous waveform data detects blocked catheter and distinguishes blockage vs. lack of flow; enables derived parameters (e.g., PVI, compliance/resistance) from waveform + circuit model.	Purely observational; only 24 h recordings; varied etiologies—needs larger/longer studies and subgroup accuracy.

table 1 continued on next page

Table 1 continued

Doppler ultrasound using ultrasonically excited bubbles	Lam et al. [11]	3–40 mL/h. Doppler system modified to measure very low velocities with ~0.5 mm/s	high correlation between Doppler-estimated and expected velocities (r = 0.992 mean; r = 0.991 maximum)	Feasibility study with in vitro flow simulation and preliminary in vivo/clinical on externalized shunts (EVD): 4 patients, 12 studies; microbubbles achieved in all 12	Noninvasive concept (no injected contrast), microbubbles maintained >10 min (and reported =40 min in clinical bedside tests) enabling ensemble-averaged Doppler; safety parameters discussed as meeting AIUM limits for the maintenance scheme.	Inconsistent bubble initiation (often needing pumping; initiation); Doppler power & spectra show large variability from bubble distribution; sample volume must be close to excitation due to the short effective bubble lifetime (~1.6 ± 0.7 s).
Radioisotope clearance from shunt reservoir (gamma detection)	Hidaka et al. [12]	0.02–1.2 mL/min (posture-dependent	Numeric value not reported.	Clinical + imaging validation (clearance patterns + gamma camera; 148 patients/231 exams)	Dynamic posture response.	High variability; reflux/leak can cause false positives.
Passive wireless resonant frequency shift (LC) linked to flow	Raj et al. [13]	Flow range: tested/calibrated 0–25 mL/h; claimed capable of <4 to >100 mL/h (Abstract/Conclusion). Resolution/sensitivity: ΔV? 0.6 mL/h (from 30 kHz f0 uncertainty).	Drift: at constant flow, <0.3 mL/h over ~1 month. Temp sensitivity: ~1 mL/(h·°C)	Bench/ in-vitro lab validation with DI water, syringe pump; wireless inductive readout (no animal/human implantation data)	Wireless passive subcutaneous readout; measures pressure + flow (twin-capacitor concept for hydrostatic/ambient compensation); good f–flow fit (R^2 ~0.999)	needs calibration; possible errors from tubing compliance/settling at low flows; hydrostatic effects require orientation/tilt correction; longer-term drift beyond 1 month has not yet been shown.
Inline thermal (single thermistor heater/sensor + Wheatstone bridge)	Qin et al. [14]	0–52.5 mL/h (temperature-specific calibration ranges used across experiments). Demonstrated accurate reporting: up to ~35 mL/h (stated from slope/accuracy interpretation). Sampling/temporal resolution: one flow value every 30 s (30 s measurement cycle).	Mean SRF/GMF = 0.98 ± 0.09 (95% CI 0.88–1.07). Bias: GMF +0.07 mL/h vs. SRF. Correlation per exp: r ˜ 0.62–0.96 (4/6 robust per abstract).	Acute in vivo (juvenile swine), inline sensor + gravimetric reference (timed collection/weighing). Usable data: 6/8 experiments.	immediate response to bolus-induced flow changes; many data points (>4300 acceptable in 6 acute exps)	2/8 failed (temp/calibration + excessive flow; hardware); higher pulse (9.6 V) minimal resolution gain but reduced longevity ? recommend =8.2 V.
Noninvasive thermal time-of-flight (external cooling pulse; downstream thermal samplers)	Rajasekaran et al. [15]	Range tested: 0.5–1.0 mm/s (CSF flow velocity in shunt tube), Resolution (Temperature probe): 0.02 °C	Paper states good agreement between simulation and bench-top results over 0.5–1.0 mm/s,	FEA (COMSOL) + preliminary bench-top in vitro validation on a simulated setup (water used instead of CSF; no skin layer included).	non-powered/portable concept for clinic use; uses Thermal Time-of-Flight with titanium couplers to overcome silicone's low thermal conductivity; bench-top results align with simulation in the tested range.	Bench-top excluded skin/tissue thermal resistance ("not taken into account"); water used as CSF surrogate; measured velocity is coupled (titanium heat transfer + flow) and requires decoupling; future work requires skin/artificial tissue and IRB for more realistic testing.

table 1 continued on next page

Table 1 continued

Implantable microfluidic thermal anemometer with RF telemetry (13.56 MHz)	Bork et al. [17]	2–40 mL/h (±10% spec at 37 °C); tested ~2.5–50 mL/h in vitro	Bias: typically 0 to - 10% vs scale (mean - 5.4% at 37 °C); temp offset: +6.3% (22? 37 °C) ? compensated mean +0.9%; drift: none over 26 days	In-vitro bench validation vs gravimetric scale using artificial CSF (2 g/L protein) ± 10% fresh blood	passive telemetry 13.56 MHz; no drift from high protein/ blood exposure.	with blood, reading orientation-dependent (sensor top ~+17%, bottom ~- 53%) due to RBC sedimentation; needs good laminar flow/alignment (one sensor ~- 12% at 50 mL/h).
Wearable thermal transport sensing over skin with BLE	Krishnan et al. [18]	Quantifiable range (modeled): 0.007–1 mL/min; physio focus: 0–0.5 mL/min.	Temp precision <5 mK	FEA + bench-top studies; human measurements (n=7).	Noninvasive wireless thermal flow sensing; foam improves SNR.	sensitivity drops with skin thickness; quantitative Q needs patient-specific skin thickness; larger clinical validation needed.
Commercial thermal liquid flow sensor (calibrated for water/IPA)	Sensirion SLF3S-0600F [20]	±2000 µL/min (±120 mL/h)	±5% m.v. or 0.5 µl/min (whichever larger)	Factory Calibrated	bi-directional micro-flow, fast (<20 ms)	saturates >±3250 µL/min, warm-up ~60 ms, accuracy depends on calibration fluid (H2O better than IPA)
Stretchable capacitive flow sensor (ventriculoamniotic shunt context)	Chen et al. [23]	0.037–0.3 m/s (velocity)	Not reported	In vitro only	Flexible/stretchable capacitive sensor; ~linear calibration; tested to 150% stretch	No in vivo test done
Charge-based time-of-flight sensing (ion cloud)	Zarrin et al. [24]	0.01–0.90 mL/min (0.6–54 mL/h)	4.2% to 7.2 %	Benchtop (saline + artificial CSF), incl. tests with a commercial VP shunt/valve assembly	low energy (37.5 µJ/measurement), compact (~2 cm), integrable.	Needs human CSF pulsatile/temperature/long-term validation.

Discussion of Clinical Translation Challenges

There are considerable advances in flow sensing technologies for CSF management devices. However, there are still challenges in translation from experimental prototypes to clinical use due to multiple challenges, including biological, engineering, safety, clinical, regulatory, and long-term performance challenges. There is a potential for biofouling, protein absorption, glial scar formation, CSF composition variability, mechanical stresses, and long-term performance challenge which needs to be addressed. Ensuring long-term biocompatibility without infection risk, thermal damage, or other damage due to electrical discharges, mechanical stress, etc. In the case of systems incorporating radioisotopes, the radiation-related risks need to be validated. Addressing these risks is also associated with adding further design constraints. Regulatory approval is also associated with identifying the risks and validation strategies. The requirement for power in some of the systems demands optimization of battery capacity and consumption. Ultimately clinical translation and better adoption of the flow monitoring systems also depend on the quality, cost, and long-term reliability of the device, focusing on not only shunt patency but also overall neurodevelopmental progress and overall quality of life.

Conclusion and Future Perspectives

It is true that the flow management system has concerns to address and regulatory requirements to be met. However, it is essential in regard of the CSF management to have better future improvements and positively aim toward successful implementation with the existing system. The progressing landscape of CSF management and flow monitoring is also associated with the new generation of advancements in sensing, wireless communication, materials, and data analytics. The upcoming systems are likely to adopt advanced sensing techniques for pressure, flow, and other biomarkers. This improves the accuracy of diagnostics. Advancements in microfabrication,nanomaterials, and flexible electronics enable the development of minimally invasive sensors. CSF dynamics can be continuously monitored and assessed using wireless telemetry; energy harvesting and low-power electronics will be beneficial for continuous remote assessment of CSF flow. Better advancements could be made in wearable devices in this regard. It will also be beneficial for pediatric and fetal applications. The use of AI and adaptive control algorithms will analyze the dynamic CSF flow and pressure data, which enables patient-specific valve regulation, predictive maintenance, and predictive intervention for shunt failure. The use of anti-fouling coatings and stretchable electronics is better for long-term stability, reducing skin irritation and interventions in the developmental stage. The use of degradable components could also be considered, ensuring that degradation won't affect the improvement of the condition during the initial developmental stages. Ultimately, the use of advanced technology aims toward hydrocephalus care that is more patient-specific and improves connectivity.

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REVIEW ARTICLE

Recall of High Risk Cardiovascular Devices – Device Categories, Device Problems and Patient Outcomes: A Literature Review

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Abstract

High-risk cardiovascular devices play an important role in management of cardiac risks and enhancement of quality of life of patients. The devices being majorly implants are in constant interactions with the human body and hence the devices have problems during the use. The problems faced by the different category of cardiovascular devices are varied. The devices are sometimes recalled for corrections when the device problems cause serious harm to the patients. The consequences of the recall of a device affects the patient in terms of safety and also becomes a threat in cases where it is a high-risk device which is implanted on the patient. The article discusses on a literature review on the category of high-risk devices, device problems and patient outcomes for high- risk cardiovascular devices. The review of literature gives an indication that there is lack of published literature in cases of device problems leading to recall especially in high-risk mechanical devices. As psychological impact is a serious concern in patients with recalled implants, more studies shall bring light to these factors and more effective management.

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Introduction

Medical devices during use in patients have different device problems. When the problems are severe causing harm to the patient population, manufacturer initiates recall of the devices for subsequent corrections (Health, 2025). The devices are recalled for corrections in the device thereby reducing harm to the patient population. After the corrections are made and it is approved by the regulatory authority the recall is terminated. Recall of medical devices happen due to different kinds of device problems specific to the kind of device. Cardiovascular devices have many reported recalls as seen from the United States Food & Drug Administration (USFDA) databases (Somberg et al., 2014). The high-risk cardiovascular devices majorly consist of mechanical devices like artificial heart valve, cardiovascular stents, Atrial Septal Defect occlusion device, endovascular graft etc and electronic devices like pacemaker, Left Ventricular Assist Devices (LVAD) and Defibrillator (Zhang et al., 2015).

Many of the studies in recall of medical devices are done based on the databases from the USFDA. The databases contain information on the approvals, recalls, adverse events, device problems, etc. (Health, 2023).

Objective

The literature review is done to address the following with regard to the high-risk cardiovascular devices:

- Different category of devices and their applications
- Device problems
- Patient impact

Methodology

USFDA have categorized high-risk cardiovascular devices as class III devices and the data on the same was extracted from the USFDA database. Search was done in Google scholar and Pubmed through different search words with regard to the high-risk cardiovascular devices, device problems, patient impact on cardiovascular recalls, safety alerts, psychological impact on recalls, device replacement, advisories on recall etc.

Results

With regard to the review of high-risk cardiovascular devices and their applications 47 journal articles were included. The device problem and patient impact further included 27 journal articles.

High-risk cardiovascular devices

Artificial heart valve

The Human heart has four different valves (Heart Valve - an overview | ScienceDirect Topics):

- Tricuspid valve which is located between the right atrium and the right ventricle,
- Pulmonary valve which is located between the right ventricle and the pulmonary artery
- Mitral valve which is located between the left atrium and the left ventricle
- Aortic valve which is located between the left ventricle and the aorta

When these valves become diseased or damaged (valve stiffness called as stenosis and leaky valve called as regurgitation) they are replaced by artificial valves (*InformedHealth.org [Internet]*, 2019), (Maganti et al., 2010), (Praz et al., 2024), (Mathew and Kanmanthareddy, 2025; Unraveling the Mechanisms of Valvular Heart Disease to Identify Medical Therapy Targets: A Scientific Statement From the American Heart Association | Circulation).

Artificial heart valves are of the following types (Mathew and Kanmanthareddy, 2025) , (Brandt' and Pibarot'), (Gott et al., 2003):

Mechanical heart valve which are made of durable materials. Since mechanical heart valves have the problem of blood clots, the patient has to take anticoagulants throughout their life time (Mack et al., 2024). The mechanical heart valves have longer life span (Traxler et al., 2022), (Zhao et al., 2023), (Korteland et al., 2017).

Bioprosthetic heart valve are made from animal tissue which is attached on a metal or polymer support. Bioprosthetic heart valve is usually made of bovine (cow) or porcine (pig) tissue and is treated through different methods to prevent rejection and calcification (Manji et al., 2012), (Rahmani et al., 2019). As these valves have less chance of blood clots the patients need not take anticoagulants (Wen et al., 2022). The bioprosthetic heart valves are less durable than mechanical heart valves.

Tissue engineered valves are also available with seeded cells on a scaffold. These scaffold act as Extracellular matrix which aid tissue growth to form the heart structure (Mendelson and Schoen, 2006), (Cordoves et al., 2023).

The heart valves are replaced by open heart surgery or Transcatheter Aortic Valve Replacement (TAVR) which is a minimally invasive procedure where the heart valve is inserted via a catheter (Srinivasan et al., 2024), (Vinayak et al., 2024).

Pacemaker

The squeezing of the heart chambers happen based on the electrical system of the heart. The electrical signals originate from the sinoatrial (SA) node, which is a small mass of specialized tissue located in the right atrium(upper chamber) of the heart. The SA node generates electrical stimulus at 60 to 100 times per minute The electrical stimulus causes muscle contraction in the heart and the heartbeat. A pacemaker is a device that is implanted on the chest to help regulate a heart that beats slowly and irregularly (Mulpuru et al., 2017), (Kusumoto and Goldschlager, 2000). The pacemaker ensures that the heart beats at a safe and desired rate. Pacemakers are battery powered and is placed under the skin near the collar bone. When the electrical system malfunctions, there is disorder in the squeezing. Pacemakers provide with electrical impulses to correct this malfunction (Lak and Goyal, 2025).

The different kinds of pacemakers are (Lak and Goyal, 2025), (Kusumoto and Goldschlager, 2000):

Single chamber pacemaker which uses a single wire to one chamber of the heart. Dual chamber pacemaker uses two wires and are attached to two chambers of the heart. Biventricular pacemaker has three wires one each connected to the ventricles and the third is connected to the right atrium. This is also called as cardiac resynchronization therapy (CRT) (Dretzke et al., 2004), (Ahmed and Kayani, 2025).

The procedure for implanting a pacemaker is usually be catheter based though leadless pacemakers are also inserted using a catheter to an inner wall of the heart (Knops et al., 2023). In transvenous pacemakers the leads are passed through the veins and it is attached in the point in the heart (Long et al., 2024), (Tjong et al., 2019). In Epicardial pacemakers the leads are placed on the outer surface of the heart (Patsiou et al., 2023).

The pace maker has three parts – the pulse generator which is a metal casing housing the battery and the electronic circuit. Leads are insulated flexible wires. The leads are placed inside the heart chambers (Ouyang et al., 2019).

Left Ventricular Assis Device (LVAD)

When the pumping of the heart is at risk due to an acute or chronic heart failure the Ventricular Assist Device is used to support the pumping of the heart. This device is a electromechanical device either used temporary till a donor heart is available (bridge to transplant) for the patient. It is also used as a permanent implant for patients not eligible for a transplant (destination therapy). Also it is used for patients during or after surgery till the heart of the patient recovers (recover support) (Eisen, 2019), (Vaidya et al., 2025). Ventricular Assist Device s are of three types : Left Ventricular Assist Device (LVAD) which is the most common type whereby the left ventricle is supported by the device to perform its pumping to all parts of the body. The Right Ventricular Assist Device (RVAD) helps the right ventricle in pumping the blood to the lungs. The BiVentricular Assist Devices (BiVAD)

supports both the ventricles (Boulate et al., 2014), (Shehab and Hayward, 2019). The Ventricular Assist Device is implanted in the chest with its cables connected to the heart's chambers and aorta or pulmonary artery.

The Ventriicular Assist Device consists of the following parts (Chaudhry et al., 2022):

- Inflow cannula connects to the tip of the ventricle enabling blood flow from the heart to the mechanical pump.
- Mechanical pump does the pumping action and is the major part of the Ventricular Assist Device.
- Outflow cannula connects the mechanical pump to the aorta (LVAD), pulmonary artery (RVAD) or both (biventricular assist device).
- Driveline or the percutaneous lead is the cable that connects the VAD through the skin to the external control device (controller).
- Controller helps in the monitoring of the VAD functioning.
- External battery pack is connected to the controller and has the main battery that powers the device and a backup. .

Cardiovascular stent

Cardiovascular stents are used to treat coronary artery disease. The arteries get narrowed and sometimes get blocked whereby the free flow of blood do not happen. Cardiovascular stents are mesh structures which are implanted at the site of narrowed artery through a catheter with a balloon. These stents are placed on the balloon and at the site the balloon and the stent is expanded. The stent is placed thereby opening the arteries and allowing the free flow of blood. The treatment procedure is termed as angioplasty. To detect the blocks in the artery, fluoroscopy is used, which is a special x ray where the contrast dye moves through the artery. This procedure is termed as angiography. A cardiovascular stent is upto around 2-inch-long and 2 to 5mm in diameter (Borhani et al., 2018).

Different types pf stents are available (Scafa Udri'te et al., 2021) – bare metal stents made of stainless steel, nickel titanium alloy, cobalt chromium etc. Drug eluting stents have drugs loaded into the stent which is delivered at the site of implantation thereby improving the healing. Bioresorbable stents gets dissolved in the artery on due course of time (Sahu et al.).

Defibrillators

When a heart rhythm is not normal it is called an arrhythmia. Arrhythmias can start at different parts of the heart and sometimes they are too fast, too slow or just irregular. Ventricular tachycardia is a kind of arrythmia where the heart beats very fast due to abnormal electrical signals at the ventricles. As the heart beats fast, adequate blood is not pumped. Ventricular filtration is another phenomenon of abnormal heart rhythm which is chaotic, severe and life threatening (Bänsch, 2012).

In both the above cases defibrillators are used to give electric shock to the heart to treat the abnormal heart rhythm. The types of defibrillators (*ResearchGate*) are:

Wearable: The wearable defibrillator is worn in contact with the chest so that the abnormal heart rhythms are detected through the sensors and electric shock is discharged to correct it

Implantable: In case of the implantable defibrillator the electric shock is given when there is a need to correct an abnormal rhythm.

Automated external defibrillator: These are designed to be used by untrained personnel and is used usually in public places or emergency situations.

Manual external defibrillators are used by trained personnel and is used in hospitals and emergency situations.

The implantable defibrillator has a pulse generator which contains the battery and electric circuits. The electrodes or leads go through the veins and give electric shock. Like pacemaker the number of leads depend on whether the defibrillator is single chamber, dual chamber or biventricular.

External defibrillator consists of the following parts (Ghzally and Mahajan, 2025):

- Power source consisting of the battery and the charging circuit
- Capacitor which stores and releases the electrical energy
- Electrodes which delivers electric shock to the patients
- Control panel for controlling the operations
- Microprocessor which determines whether an electric shock is required

Atrial Septal Defect (ASD) closure device

Atrial Septal Defect is a congenital heart disease where there is an abnormal opening in the wall separating the heart's upper chambers. This causes the blood to flow between the chambers. ASD closure devices are used to close this hole. It is a minimally invasive procedure and the device is delivered through a catheter (Fraisse et al., 2018).

ASD closure devices are made of wire frame of nitinol (nickel and titanium) with a covering of fabric. The device has a left atrial disc and a right atrial disc with a short waist. This waist shall correspond to the size of the hole. The device is sewn by a polyester fabric material to ensure secure occlusion (Jung and Choi, 2018).

Endovascular graft

Like stents, endovascular grafts are also used for aneurysm repair. Endovascular grafts are combination of stents and grafts where a fabric is attached to the stent. When the stent provides structural support the fabric material attached to the stent acts as a new vessel wall thus reinforcing the deseased area.

The greatest effect of using endovascular graft is aortic aneurysm repair.Fenestrated Aortic Aneurysm Repair (FEVAR) is a technique that repairs complex aneurysms with openings that allow blood flow to branch arteries thus preventing the aneurysm to grow bigger (Marin et al., 2003).

Device problems - cardiovascular high-risk devices

The studies which describe on the various failure modes in the cardiovascular devices are very few. In the study (Yang Hu a and Pezhman Ghadimi, 2024) the failure modes of medical devices during 2018-24 are analysed calling them "Recall initiators". The major failure modes are device design, process control, non-conforming material/component, software design etc. Failure of the design is seen as a major reason for recall in some of the studies (Claudia See 2024), (Teodora Miclău 2019). There are no studies wherein the failure modes are analysed and the correlation to recall is assessed.

Majority of the discussions on device problems for high-risk devices which has led to the recall are on electronic devices like pacemakers and defibrillators. Device problems for defibrillators and pacemakers like premature battery depletion caused by Loss of hermetic seal in battery, Bonding wires separating from terminal, Software error, Moisture ingress through header, High internal battery impedance, pacing problems are discussed (Mikhael F. El-Chami, 2026), (Robert G.

Hauser MD N et al., 2006),(Robert G. Hauser MD N et al., 2006), (Jay Sengupta and et al, n.d.), (David C. MacGregor M.D. et al., 1977). Other battery problem also include high internal cell impedance (HICI) in its lithium batteries that caused the devices to revert to the Safety Mode (SM) during higher power operations such as telemetry (Robert G. Hauser MD et al., 2025). Leads are reported as the weak point of cardioverter defibrillator system and defective leads become reasons for recall (Maria Grazia Bongiorni, 2014),(Journal of Cardiovascular Electrophysiology et al., 2010). Software related battery and cybersecurity issues have been seen as a highly relevant reason for recall as use of internet connected implants is increasing (Bridget M. Kuehn, 2018). Generator failure is another cause for recall in defibrillators and pacemakers (Jerome Schwartz et al., 2010), (William H. Maisel et al.).

The device problems in cardiovascular stents indicate major occurrence like migration and activation failure (Yuchi Ma 1 et al., 2022), (Jonathan D. Marmur, MD, FACC et al., 2014) fracture of stent and defect of balloon (Zhang et al., 2015), sterility, impaired delivery of stents (Sanjay Kumar et al.), separation of delivery system , problems with balloon deflation (Donald S. Baim, 2006). The problems reported in the various literature on the recall of Left Ventricular Assist Devices include battery malfunction, loose driveline connector, malfunction of the system controller, loose power supply connector ports, malfunction of the driveline splice kit, problems with the percutaneous lead connection, disconnection of the bend relief & outflow graft and outflow graft occlusion (Diego Lugo Baruqui 1, 2020). Heart valves were prone to device problems like paravalvular leak degeneration or mechanical failure (Frederick J. Schoen 1 et al., 1985). One recall is reported on allograft heart valve raising concerns on the processing of tissue leading to infections to the patients (Dorothy Bonn, 2002). Design related issues are reported in the recall of bioprosthetic valve where a silizone coating on the valve is given to provide with a novelty edge to the product but the product had poor performance (I. Vesely, 2003)

Patient impact

The psychological impact on the patient on experiencing recall of an implant is explained that “recalls do not affect all ICD patients equally, with risk factors for poor psychological adjustment to Defibrillators including younger age (<50 years), shock experience, and female gender that may be associated with increased recall anxiety.(Samuel F. Sears Jr. PhD, 2006). The study expresses the concern that the “faith “ in the device may be changed. Specific fears and symptoms of anxiety are faced by the Defibrillator patients. Studies report that through the constant support of the clinicians, support groups - both local and virtual, information is passed on to the patients that may reduce the anxiety of the patients. (Samuel F. Sears Jr. PhD, 2006). Some studies also conclude that there is no significant difference on the psychological factors on patients who had defective implants versus with normal ones.(Douglas P. Gibson , et al., 2008). There are also reflections that the confidence of patients deceased significantly on learning on recall. Caregivers also were affected and showed lesser confidence on the device (Sneed NV 1 , et al., 1994). Studies also discusses that pre and post counselling in the patients with defibrillators and concludes that the patients concerns on recalls can be reduced by appropriate counselling (John D. Fisher, 2009).

Discussion

Comprehensive literature is available on the different category of high-risk car-

diovascular devices indicating the different types under each category, applications and components. The different category of devices clearly depicts the significant contribution in treatment of trivial heart diseases and also reveal the advancement in technology of medical devices. Studies on the device problems are majorly seen in the case of defibrillators, probably as this is the largest recalled in case of high-risk devices. However the reviews /studies on device problems for mechanical devices like heart valves, occlusion devices, coronary stents, endovascular grafts are few. The US FDA database has sufficient data on the recall, device problems and adverse events on these devices. Conducting retrospective studies on these databases would give the clinicians, and manufacturers inputs on the device problems which would help in the management of recalls and also on risk management measures during the product development. Many studies report on the patient-clinician communications in case of the recall management, which is suggested as a good measure to decrease the anxiety and fear on the recall. Strategies by the manufactures and regulatory in communicating the recall through the clinician is not seen well recorded in the literature. This indicates the need to have studies involving clinicians on awareness on the recall of devices , recall management procedures, managing the psychological stress factors of the patients etc.

Conclusion

Recall is a very important measure taken by the manufacturer and the Regulatory to minimise the harm to the patient. The literature review provides with an insight that there is a scope for more studies for recall of medical devices especially on device problems and patient impact of recalls. Detailed studies on device problems and adverse events shall provide the manufacturers with inputs for implementing risk management strategies. Clinician shall be aware of the device problems and how the same can be addressed.

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