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PVDF-based Sensors for Cardiology and Cardiovascular Therapy or Theranostics

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Abstract

This short bibliographic paper is convolution / quintessence of the chapters from a non-English monograph “Applications of frerroelectric polymers in technology and medicine - complex review” (printed in Moldova in 2021, and, unfortunately, inaccessible to the English-speaking readers), considering application of PVDF-based materials for sensory purposes and especially focused on the methods and techniques related to hemodynamics, blood biochemistry and cardiology / cardiovascular therapy.

Keywords: Cardiovascular therapy; Ferroelectric polymer; Piezoelectric polymer; PVDF; Surgical meshes; Hemodynamics; Photoplethysmography; Korotkoff sounds; Cutaneous blood pressure sensors; Cardiorespiratory signals; Point-of-care sensing and diagnostics; Blood ammonium analyzers; Hemocompatibility; Angiogenesis; Vascularization; Meshes

PVDF-based sensors of cardiorespiratory signals, blood pressure and heartbeat sensors

This short bibliographic paper is an extended convolution / quintessence of the chapters from a non-English monograph [1] (unfortunately, inaccessible to the English-speaking readers), considering application of PVDF-based materials for sensory purposes and especially focused on the methods and techniques related to hemodynamics, blood biochemistry and cardiology / cardiovascular therapy.

Sensors for both fundamental physiological and biophysical parameters and a number of important clinical and biochemical parameters based on PVDF are well known since 1970s-1980s. The most popular examples of physiological and biophysical sensors based on PVDF include:

1. Blood pressure sensors: both cutaneous blood pressure sensors (including those analyzing Korotkoff sounds [2]), and intravascular pressure sensors [3]; both based on the conventional principles of piezoelectric transducers [4,5], and non-invasive sensors based on the principles of photoacoustic measurements and photoplethysmography [6].

2. Piezoelectric blood flow sensors [7,8], including Doppler blood flow sensors [9], non-invasive blood flow sensors for transcranial and intracranial measurements [10]; and in general - hemodynamic sensors, including photoacoustic ones, especially tomographic devices using PVDF sensors [11-14].

3. Integrated multichannel monitors of cardiorespiratory signals, including intraoperative and bedside clinical monitors and sensors [15-17], as well as fetal ones for monitoring intrauterine development [18].

4. Heartbeat [19-21] and / or pulse sensors - mainly contact wrist and finger ones [22] or non-invasive models [23-25] (including echo-sensors [26]); both with wired transmission [27-29] and wireless telemetry; often self-sustaining by powering pulse energy converted into electrical one using PVDF piezoelectricity [30,31]; in some cases sensors for arterial measurements, including intraoperative and perioperative ones [32,33].

PVDF-based sensors for measuring blood biochemical parameters

The most important sensor systems for measuring blood biochemical parameters using PVDV include:

1. Composite membranes (for example, PVDF-Nafion [34]) and fiber [35] blood glucose analyzers, mainly based on

photoelectrochemical [36] and photoacoustic principles [37-40] with the main difference being either enzymatic or non-enzymatic detection principles [41-43]).

2. Blood ammonium analyzers, including POC-ones (which can be used at the patient's bedside - "point-of-care") [44].

3. Sensors for single physiologically relevant ions, for example, for potassium ions, based on the principle of a PVDF-HFP optode [45].

Implantable and longitudinally usable PVDF-based sensors in cardiometry, actuators for cardiovascular therapy and they "futuristic" problems

A fundamentally new biomedical engineering trend, actively developing in the 2000s-2010s, is the design of piezoelectric thin-film pressure sensors based on PVDF-TrFE for use in catheters [46,47]. Such electrically controlled systems are used in the treatment of different cardiovascular pathologies, including thrombosis and atherosclerosis [48].

Unfortunately, at the end of the 2010s. this research area has moved from the field of pure medicine to the field of robotics [49], which has raised many ethical questions that make constructive development of this topic impossible. Indeed, in the medial areas related to the functions of the human body, it is necessary to clearly distinguish between the obligate (from a physiological point of view) functions that require maintenance at the cost of intervention and installation of a permanent life-sustaining system into the human body (for example, artificial heart valves or insulin pumps for patients with diabetes), from the voluntary goals of postmodern medicine, lying in the area between plastic surgery and the "improvement of nature" of a person, leading to the creation of a "superman", "cyberman", etc., but in fact crippling a voluntary patient due to the irreversibility of the aging processes of both the human body and the active material implant.

In our opinion, such long-term solutions are acceptable only in the case of a decision between life and death, for example, in cardiac implantology. A similar remark concerns the prospects for the introduction of PVDF-based piezoelectric microrobots and nanorobots, which already have laboratory and sometimes veterinary-tested prototypes [50].

Biocompatibility problems in biomedical engineering of PVDF-based sensors: from hemocompatibility in angiogenesis and vascularization to biophysical or electrophysical biocompatibility of biomedical constructs

For such applications involving prolonged contact of PVDF-based material with biological tissues, biocompatibility is necessary. For the purposes of hematology, cardiac surgery, and vascular surgery, it is necessary to ensure hemocompatibility. There are currently many works on the hemocompatibility of PVDF and its copolymers, which proves the fundamental consistency of the attempts to use this material in contact with blood, both for extracorporeal applications and for implantable materials and devices [51-64]. There has been a certain increase in interest in this topic recently, leading to the appearance of many works on hemocompatibility of such compositions per year [65-68]. Conceptually, the level of work in this area remained unchanged for a long time, but the novel zwitterionic approach to hemocompatibility [69-74] appeared in the 2010s. has led to the new opportunities in this field.

In a broader sense, we should speak about tissue biocompatibility when ensuring angiogenesis and vascularization [75,76]. It is known that vascular grafts or vascular endothelial fouling implants using PVDF [77-85] have been actively introduced since the 1990s. Also in vascular surgery PVDF threads [86], fibrillar patches [87] and meshes [88,89] are already used, while in the future theranostics PVDF-containing medical piezoelectric textiles (in intraoperative, perioperative, and implantable forms [90,91]) will be widely applicable. It is obvious that for all such implantable materials and tissue-engineered structures based on them biocompatibility is a necessary prerequisite for their successful applicability in practice.

The crucial features of PVDF and its copolymers with piezoelectric properties for applications in cardiology and cardiovascular therapy include:

a) The possibility of using them as actuators and sensors simultaneously.

b) The possibility of a direct energy capture necessary for the sensor operation by its material (PVDF), for example, in contact with an artery [92,93].

c) Compliance with the acoustic impedance of water, which constitutes a significant volume of any living organism.

Consequently, to create hemodynamic and other cardiovascular sensors based on PVDF, it is possible to use biocompatibility criteria according to energy / electrophysiological, acoustic / electroacoustic and vibroacoustic criteria. It is noteworthy that, according to the latter criteria, the possibility of introducing PVDF in medical practice is much greater than that for the solid-state sensor and actuator materials, since PVDF has lower quality factor and good frequency tuning.

Prospective applications of PVDF in multi-angle measurement and mapping in angiography and optoacoustic tomography

It is known that position-sensitive sensors and ultrasonic sensors with angular resolution (including convex type ones) are also built on the basis of PVDF. Therefore, it seems possible to integrate ultrasonic and photoacoustic / optoacoustic position-sensitive detection methods with telemetric wireless signal transduction and recharging from the body's own vibrational and electrophysical signals (using PVDF-based local implantable devices). A significant technical basis for the integration of photoacoustic methods of vascular analysis (angiography and

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optoacoustic tomography), focused ultrasound methods and ultrasound analysis of hemodynamics has been accumulated since the 1990s [94-105].

Still unresolved problems and approaches that have not yet been introduced into the mainstream medicine

All the remaining problems are technical in nature. The above described devices, including intraoperatively implanted telemetric systems - "chips" for monitoring the individual functions of the body's blood supply, may appear in the nearest future, but their use also raises many bioethical problems, in particular the problem of personal biometric data (especially when they are transmitted over an open channel within the framework of the publicly accessible telemedicine). On the other hand, their appearance raises bioethical questions in terms of the minimally invasive/non-invasive nature of the corresponding control methods [106] and the risk of vascular embolism or clamping of the blood tracts with the corresponding devices [107].

For more details the readers can refer to the recent review [108], the chapter from the book [109], as well as the series of reviews started by the article [110] (which has already received a number of positive reviews in biomedical and biotechnical periodicals [111,112]).

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