(Online) ISSN 2744-1636
Bioengineering Studies *Review Article*
Vol. 6, No. 2, 2025, pp.20-32
https://doi.org/10.37868/bes.v6i2.id323

Organ-on-a-chip (OOC): a novel, straightforward, and efficient strategy for in vitro research

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Received Oct. 3, 2025
Revised Oct. 29, 2025
Accepted Dec.16, 2025
Online Dec. 31, 2025

Abstract

Organ-on-a-chip (OOC), known as tissue chips have drawn significant interest because of its various applications, particularly in drug development and screening. These devices can reduce the need for in vivo animal studies and offer useful alternatives to conventional preclinical cell culture techniques. The conventional in vitro test used to evaluate absorption, metabolism, distribution, toxicity, and excretion (ADME) was transformed by the rapid advancement of OOC technology. Numerous biomedical applications have emerged as a result of dramatic advancements in OOC design technology over the past few years. Additionally, these advancements have revealed new opportunities and challenges. Scientists all over the planet are advocating for the consolidation of OOCs for ADME and toxicity assessment. There is a requirement for multidisciplinary information from the biomedical and design fields to comprehend and acknowledge OOCs. OOC is more advanced than conventional 2D culture systems thanks to its precise flow control systems and quick sample processing. It provides a platform that mimics human physiological functions. The advantages and disadvantages of biomedical approaches are highlighted, as well as current applications, toxicity evaluation, and a snapshot of this rapidly evolving technology in this review.

Keywords: Organ-on-a-chip; human body; microfluidic chip; 2D and 3D cells; in vitro model

1. Introduction

Organs-on-a-chips, also known as OOCs, are systems in which artificial or human-made miniature tissues are grown within microfluidic chips [1]. The precise manipulation and processing of microscale fluids is the focus of the science and technology of microfluidics [2]. Its small dimensions, large surface area and high mass transfer make the microchannel ideal for applications in microfluidic technology where precise control of physical and chemical properties, low consumption of residues (constant liquid or dissolved solids), controlled volumes with high mixing speeds, and fast responses are important [3]. Microfluidics coordinate examples are planning, responses, partition, identification, and fundamental working units, for example, cell culture, arranging and cell lysis [4]. For coordinating and controlling little arrangement volumes, the chip is planned as a microfluidic gadget with half-fine microchannel networks [5]. Thus, interest in OOC has escalated. OOC is a biomimetic system that has the ability to control important variables including concentration gradients [6],

pattering of cells [7], and interactions between organs and tissues [8]. Furthermore, it has the ability to simulate an organ's natural environment. The main goal of OOC is to encourage the physiological environment of human organs. Human physiology is the study of the functions and organ systems of the human body [9]. This has a significant impact on understanding how the body malfunctions and how disease develops, and it has implications for toxicology, drug development, and medical practice [10]. The most relevant and direct way to study human physiology is through in vivo experiments on actual people or model organisms. For drug development and toxicology, the physiological effects of tens of thousands of compounds must be assessed. Biologists use *in vitro* cell culture because low-throughput in vivo testing has limitations. Cell culture refers to the growth and maintenance of cells in a regulated environment [11]. For many years, traditional two-dimensional (2D) cell culture systems were the support of life science research. By culturing cells or cell products, various cell functions can be studied with 2D systems. Due to their inability to precisely imitate the physiological pointing of living tissues and organs as well as the microenvironmental factors, 2D systems often ask for verification *in vivo* animal models [12]. The OOC can be viewed as a connecting technology because it enables the use of sophisticated cell cultures and improved designed microenvironments to enable the model to function at its best.

While the term OOC proposes that smaller than normal organs are developed on a chip, it is essential to take note that this slippery objective has not been accomplished. All things considered, these frameworks contain little tissue builds intended to replicate only one or a couple of explicit practical properties of the whole organ. The simplicity of these models, which is a major advantage, allows direct assessment of the effects of genetic and environmental factors on function of tissues and cells. OOC construct matured tissue structures that demonstrate distinct organ functions using bioengineering tools. According to the many excellent reviews that have recently been published [13], research in the fields of OOC and microphysiological systems has increased at an outstanding rate after animal-on-a-chip [14], body-on-a-chip [15], and breathing lung-on-a-chip [16]. OOC technology is now recognized far beyond the walls of university laboratories due to the need to better understand the human physiology that underlies health and disease as well as to find new approaches for improving human behavior. OOC innovations have progressed and developed considerably, and it is anticipated that interest will keep on filling before very long.

OOC has several uses, but the most important one is in the development of drugs and the effects they have on diverse organs. The majority of drugs are tested on animals, which occasionally results in inaccurate results or raises ethical questions from organizations like People for the Ethical Treatment of Animals (PETA), but is still considered as a critical step in tumor research [17]. According to Wikswo et al. and Marx U., this prompted researchers to look for novel approaches that would permit testing on human cells [18]. The OOC concept is forward-thinking because it uses a "little me" (customized chip) on which different medications can be tested on a framework similar to that of the patient. This makes it possible to find the right medication without harming the patient, while also enabling the selection of the ideal treatment that would be beneficial for the selected OOC plan [19]. In the long run, this technology may be used to develop personalized medicine strategies that successfully treat individual patients by utilizing their own cells. Replicating the behavior of tumor cells in these OOC allows for cancer cell behavior analysis, as well as the chance to test hypotheses and gauge results in order to create new therapeutic approaches [20]. In recent years, microfluidics has advanced to the point where drugs are tested for viability in a lab-on-a-chip. The drug uses field OOC to identify and classify various medications atoms in terms of their quantity and quality. Some of the limitations of the drug test have been relaxed, allowing for the use of new applications like drug testing, control of drug quality, and precise medication [21].
Cells and animal models still dominate international drug screening. Day et al. point out that the bodies of animals and humans differ in particular ways [22]. 2D human cell models in vitro, an alternative that is also traditional, cannot consider the mechanical stresses and intricate microenvironments that are present in vivo [23]. There are distinct limitations to each of these conventional screening methods.

The primary structures, distinctive functional traits, and complex organ-to-organ connections of various tissues and organs can, however, be encouraged in vitro using an organ-on-a-chip. To create chip systems with various structures and multi-organ couplings to meet various research needs, key technologies including 3D bioprinting, microfluidic chips, and microfluidic cell cultures can be used. Bittner et al. claim that the patient's own body can be used to print customized tissues and organs [24]. The dilemma that drug developers have had to choose between traditional in vitro and traditional in vivo methods—both of which have their limitations—may now be resolved thanks to these unique benefits. Organs-on-a-chip may enable targeted neurotic research, organ-to-organ crosstalk studies, and closer examination of the elements of medication activity and damaging effects behind illnesses, lowering the cost of medication screening and accelerating drug development work.

2. OOC design components

The OOC includes four crucial components: 1) microfluidics; 2) tissue with living cells; 3) drug administration or stimulation; and 4) sensing [25]. The microfluidic component is what uses microfluidics to move target cells to a predetermined spot. This component also includes a system for the flow of waste liquid and culture fluid throughout the culture process. The attributes of this component are automation, integration, and miniaturization [26]. A "living cell tissue component" is a part of a 2D or 3D system that aligns spatially a specific type of cell". The addition of biocompatible materials like hydrogels typically results in the creation of the three-dimensional arrangements. These materials can shape three-dimensional arrangements and prevent mechanical damage. Living cells in organ tissues are still primarily grown in 2D due to technical and financial constraints, extracellular matrix assembly, and the presentation and formation of vasculature. To stimulate physiological microenvironment, which promotes microtissue maturation and function, for some tissues, physical or chemical signals are needed. Compared to 2D models, the 3D tissue structure more closely simulates the *in vivo* setting. Peel et al. utilized mechanized frameworks to picture multicellular OOC, delivering point by point cell aggregates and factual models for estimations [27]. Kane and associates. developed a cell framework to test the cells in a 3D microfluidic environment [28]. Without microsensors-enabled analysis of the metabolic state at distinctive focuses in the framework, a significant human-on-chip cell model cannot be portrayed and reached.

2.1. Concept for design

Control of the external and internal cell environment is necessary for culture systems [29]. OOC, in conjunction with micromachining and cell science, has some control over external boundaries and precisely animates physiological environments [30]. On the chip, it is anticipated that there will be dynamic mechanical pressure, liquid shear and focus angles. To fully reflect physiological processes, cell patterning must also be realized. Through miniature siphon perfusion, which helps with the organization of supplements and ideal disposal of waste release, microfluidic technology enables the powerful culture of cells. The location of the cells in changing environment is more similar to *in vivo* conditions than rigid culture. Fluid shear stress also causes the organ to become polarized [31].

OOC applies fundamental actual tension to the typical organic elements of endothelial cells [32] by enacting cell surface particles. The OOC framework summarizes course using either a simple "rocker" on a chip smooth movement or a more complex programmable "pulsatile" design that is organized in a single circle for association explicit setup [33]. At the microscale, the liquid primarily behaves as a laminar stream, causing a steady inclination of biochemical particles that are both spatially and temporally controlled. By adjusting stream speed and channel math using microvalves and tiny siphons to achieve steady, 3D biochemical fixation angles, microfluidics animates complex physiological cycles in the human body.

In order for the human body to function properly, its organization necessitates the precise and intricate arrangement of numerous cells. *In vitro* physiological models with intricate geometries can be constructed using microfluidics to control cell patterning. Surface alterations and 3D printing enable patterning of cell on the chip [34]. The benefit of 3D printing is to permit client characterized advanced covers to give adaptability in cell designs, basic for the in vitro remaking of the cell microenvironment.

2.2. OOC's Strengths and Weaknesses

The idea of organs on a chip has several advantages, the first of which is the potential for accelerated research [35]. Due to the relatively low cost of producing the chips, multiple medications and dosages of medications can be tested at the same time without the need for specialized equipment [36].

This could be useful when a new drug is found that does not need test subjects and does not appease ethnic concerns. Because of their small size, multiple microfluidic systems can be combined on a single chip, saving both space and money. Imitating the tissue and organ microenvironment are another benefit. Contrary to conventional 2D cell culture, organ-on-a-chip systems allow for the controlled co-culture of different cell types to mimic the various structures and functions of tissues and organs, such as the heart, lung, and brain [37]. By simulating the microenvironment of cells with respect to physical and chemical signals, organ-on-chips allow cells to maintain specific tissue characteristics that could be changed in conventional 2D cell culture. Additionally, organs-on-chips can directly develop human cells for radiobiology studies, avoiding the need to use animals and the associated barriers based on species. For instance, carrier proteins are supposed to avoid the species-to-species variations in hereditary articulation profiles [38]. As is common knowledge, organ-on-chip technology uses similar microfluidic frameworks to those found in the lab-on-a-chip industry. This could directly integrate organ-on-chip cell culture systems and lab-on-a-chip systems that allow physiochemical characterization. Low-dose radiation has the potential to kill some necessary cells and result in serious embryonic diseases, despite the fact that it is currently undetectable. In any case, early incipient organisms and undifferentiated cell determined undeveloped tissues can be refined and radiation illness can be investigated with the aid of organ-on chips [39]. Because age, gender, and genetics all have an impact on how radiation affects each individual, it is important to study the individual radiobiological effects [40] [41]. This is helpful for improving specific chemotherapies as well as understanding the mechanisms by which low-dose radiation causes bioeffects. The correlation between the chip's cellular responses to the real organs and the chip's level of radiation damage are technical key points. The evaluation of radiation damage can benefit from the incorporation of biomarkers [42], genomic analysis [43], and physiological responses into the chip [44].

Surface impact is the main annoyance that is considered. Since the components of liquids are so small, surface effects outweigh volume effects. This might show in the examination's low quality and lead to some of the interesting findings being adsorbed. It's possible that the relevant fluids won't mix properly due to the presence of laminar flow at the intersection of multiple fluids. One more constraint is addressed by the way that, in certain trials, there is a requirement for extraordinary instruments to get solid outcomes [45] Additionally, as is known from their use in disease modeling and drug research, organs-on-chips are currently not appropriate for studying long-term effects because a disease may progress for years. To study the long-term diseases brought on by low dose radiation, organon- chip culture times of weeks [46] are currently insufficient. Organ-on-chip systems should not be used to study chronic diseases caused by low radiation. What's more, low-portion radiation might prompt mental debilitation, which can as of now not be concentrated on in organ-on-a-chip frameworks.

3. Materials Required and External Equipment

The choice of material is influenced by a number of factors, such as the final device's utility, microfabrication technology, readouts, and biocompatibility. The final OOC gadget is made from a variety of material assemblages. One of the most widely used materials is silicon rubber, such as poly (dimethyl siloxane) (PDMS). Additionally, there is glass and thermoplastics like PS, PMMA, PC, or COC (cyclic olefin copolymer). There is no perfect standard material, though, because of the benefits and drawbacks of the various materials. Choices are with respect to material decision are many times a split the difference between wanted usefulness, admittance to creation offices and improvement phase of the item. Glass is powerful and dormant, yet costly and requires progressed handling offices. Making complex nanostructures for on-chip sensors or graters for barriers with silicon is possible, but it is difficult and expensive because clean-room facilities are required [47]. Because it is opaque, standard inverted microscopes cannot be used with it. Although thermoplastics ensure transparency and are easy to mass produce, they pose challenges when creating intricate designs during the prototyping stage.

PDMS is currently the material that is used the most frequently for improving OOC devices because it makes it easy to produce devices with high-quality micro- and nanostructures [48]. Because of its biocompatibility, optical simplicity, and gas penetrability, PDMS is excellent for organic applications [16]. Cells have been subjected to mechanical excitement thanks to PDMS's versatility. This material is known to retain a wide range of (bio)chemicals, which could affect test results, particularly for applications involving drug testing [49]. In order to solidify the liquid PDMS, a substance that helps with that process is added during the manufacturing process. A mold is then filled with mixture to create the chip. The body can be adhered to another chip or left alone after the mixture has solidified the chips. Because of many of its properties, the PDMS became popular. Because it is transparent, the user can see how the OOC works. Because it is inexpensive and known to be less toxic, the material is simple to use. As 3D printing innovation progresses, a few gatherings have detailed OOC models produced by 3D printing [50]. This method enables the rapid and precise construction of complex 3D structures that were previously challenging to realize with the other approaches discussed so far. The lack of optical simplicity currently prevents the use of 3D-printed microfluidic devices for OOC applications because pitch definitions and post-handling procedures have not yet advanced for this property. Verification of 3D-printed resins' biocompatibility is also required. OOC technology has progressed to the point where efficient fabrication techniques can be used by choosing materials based on experimental needs. The OOC needs to be made of a material that doesn't affect the parts of the cellular microenvironment and keeps the fluid connection stable [51].

Different biomaterials are anticipated to produce excellent results because every organ is built differently. For instance, collagen is generally utilized as a result of its benefits, yet it needs some mechanical help without which the collagen stays in one piece for a brief time frame. To get the best results, external equipment is needed. Controlling the micro and nanofluids' external flow is the first step. Ho et al. use pressure generators and a variety of pumps for this purpose [52]. Using hydrostatic pressure to control flow is the most effective method. Pressure generators, which typically include a pressure source like a compressor, pressure regulator, and pressure generator, are equipped with a monometer that is used to measure the current pressure value [53]. Despite the fact that the framework is straightforward, it has significant mishaps for the most part contained in its restricted reaction time. There are workarounds for this problem, including the use of pressure multiplexers, which make changing the pressure much quicker. The addition of flux sensors, which convert the control signal from pressure to flow, is another way to enhance pressure generators [54]. After a certain number of days, the cell culture's viscosity and density change. This must be kept in mind when building the chip, as studies indicate that the analyzed models experienced significant wall pressure and increased stress.

3.1. External Equipment

3.1.1. Flow control

Another system that is typically utilized for flow control is pressure syringes. They are typically utilized in perfusions, but microfluidic research has also adopted them. They enjoy the benefit of having the option to control the stream without being impacted by annoyances brought about by liquid obstruction. Similar to the pressure generator, the flow pulses use small values, which results in a long setting time **[55]**. There are two different kinds of pumps used to regulate flow. The first is a straightforward liquid pump with a nonlinear model that has some limitations. The framework normally requires a decent sensor to recognize little stream vacillations. Electro-osmotic pumps, on the other hand, are resistant to high counter pressure and do not experience flow fluctuation issues **[55]**. However, they have the drawback of requiring low conductivity liquids for proper operation.

3.1.2. Sterilization

The 3D architectures and materials of OOC devices set them apart from conventional platforms for cell culture [56]. Performing cell culture in OOC gadgets has comparable necessities with customary stages. The requirements for OOC devices' sterility are comparable to those of conventional platforms. Therefore, the OOC

devices, including the various microfluidic parts that will be used to set up the entire OOC system, must be sterile in order to prevent microbial contamination. The variety of materials used in OOC devices and microfluidic components necessitates extra caution when selecting the best disinfection techniques to prevent damage. By damaging OOC devices and microfluidic components, improperly applied sterilization techniques can cause unintended leaks during system assembly [57]. Many plastics, including PMMA and PC, may not be suitable for conventional autoclave sterilization due to their low thermal resistance. Different strategies for disinfection, like UV or ethanol treatment, are in many cases utilized in the research facility setting, although these techniques ought to be utilized with alert. The material's ability to retain germicidal UV beams and murkiness may limit UV entrance. Some materials, like PMMA, may disintegrate to some extent during ethanol drenching, making it ineffective for those materials. Ethanol can be absorbed into PDMS components after being soaked for a long time, and when it is leached out, it may have an impact on cells. In clinical or industrial settings, ethylene oxide treatment and gamma irradiation ought to be the sterilization methods of choice [57].

3.1.3. Surface preparation

Device surfaces that encounter other cells might need to be treated to ensure biocompatibility or bolster cell adhesion. In 3D spheroid or organoid cultures, Pluronic acid is frequently used to passivate the surface of the chip in order to prevent unfavorable spheroid or organoid dissociation via potential cell attachment [58]. This is important because losing the 3D tissue design could negatively impact an organ's ability to function physiologically. However, if we want to improve cell adherence to the chip substrate, protein and extracellular grid (ECM) coatings may be used. In the gut [59] or blood-brain barrier (BBB) OOCs [60], attached, confluent monolayers of cells are required for the replication of the intestinal epithelium and the endothelium, respectively. Tissue- and disease-specific matrices can be utilized to create (patho) physiological models with a higher degree of fidelity [61]. These may contain biomatrices made of collagen or fibrin. Cells can be combined with the liquid form of these biomatrices, loaded into the OOC device, and allowed to polymerize into a gel. Some organs, like the liver and skin, require a 3D microenvironment to function normally, and biomatrices can be a helpful scaffold for cells to remodel into a 3D structure [62]. Biomatrices may also be crucial for maintaining or separating particular cell types.

4. Utilization of OOC

4.1. OOC for screening drug efficacy and toxicity

The method of developing a drug takes a long time and costs money. The inaccessibility of a legitimate framework mirroring the intricate human physiology frustrates the outcome of medication up-and-comers entering clinical preliminaries. As a result, very few are making it to the market [63]. Standard two-dimensional cultural systems or animal models, which are thought of as the gold standard in toxicity screening, have a great deal of limitations and uncertainties attached to them. A cell experiences constant blood perfusion, various substances, mechanical and electrical sensations, and cell and cell-lattice interactions in the local in vivo environment [64]. The conventional two-dimensional cultural system lacks it. Compared to animal cells, human cells react differently to chemical molecules. A technique to provide the complex microenvironment of cells and tissues is needed in order to accelerate drug discovery and anticipate possible responses.

The establishment of an exciting platform known as OOC, which allows for the creation of functional tissue constructs while taking into account the dynamic microenvironment, has been laid by the development of microfabrication technologies and tissue engineering [64]. OOC provides a drug concentration gradient that is physiologically relevant in comparison to a 2D culture assay. This platform makes it easier to determine a drug's anticipated and unanticipated toxicity. It can also be used to assess the specific poisonousness of a species. The advantage of the microfluidic device includes the requirement for low reagent volumes, common supplement bioavailability, oxygen supply, and control over extracellular microenvironment than the conventional macroscale cell culture tests empower them as an attractive instrument for illness demonstrating [65]. By

controlling the ratio of extracellular to intracellular fluid volumes over time, a paradigm shift in drug development is made possible [66].

4.2. Biological application

The creation of multi-OOC systems to imitate the human body's systemic physiology is one broad area in which we can anticipate continued innovation. This application, which was initially created to evaluate the efficacy and safety of pharmaceutical compounds, is expected to be expanded to include additional therapeutic agents, such as nanomedicine, alternatives to engineered tissues, and cell treatments. Immune cells are found in every body tissue, and the health and pathology of those tissues are determined by their homeostasis [67]. As a result of the development of immunotherapies and improved protocols for expanding and maintaining immune cell populations in vitro, there is an increasing push to incorporate both adaptive and innate immune components into OOC systems [68]. With regards to disease immunotherapy, scientists have begun using OOCs to examine malignant growth cell-resistant cell collaborations in 3D conditions [67]. In order to investigate how cancer cells alter the tumor microenvironments, efforts are also being made to create lymphatic vessels within OOCs [69]. The intricacy of the invulnerable framework presents many difficulties as well as any open doors. Efforts to meet these needs range from biomaterials that mimic natural immune responses [70] and are easily incorporated into any cell culture to sophisticated long-term OOCs that mimic disease and include various types of immune cells [71]. Organoids-based OOC systems provide an unprecedented opportunity to study patient diversity as a biological variable, including age, sex, disease state, and patient-specific studies of disease progression and treatment effects. OOC frameworks need to fundamentally modify their plan and aspects to oblige enormous performed organoids [72] or contribute significant endeavors to adjust and enhance separation conventions for in situ organoid separation on-chip [73]. OOCSs comprise of moderately basic tissues, contrasted and their local partners, they can be inexact on or hardly any organ-level capabilities: lung barrier function, hearth contractile function, or kidney filtration. Because they provide experimental control in human tissue settings and biological fidelity, OOCs have the potential to become widely accepted in biological research.

5. OOC examined organs

Compared to their function in the human body, organs are made up of various types of cells [74]. Because different cell types serve different functions, the structure of the cells in different organs varies. According to Mertz et al., the OOC must be constructed in a manner that is most appropriate for the microenvironment in which the cells conduct their experiments [75].

5.1. Liver

The liver, which carries out a number of tasks to maintain typical physiological processes, is one of the most crucial organs in the human body [76]. It has a tremendous capacity for regenerative regeneration, which enables it to recover from any harm that may be inflicted upon it by chemical or physical means. The majority of injuries are brought on by adverse drug or disease reactions, which may be too severe in some instances. There were few excellent in vitro models before the OOC technology. The majority of the rugs underwent in vivo testing on animals. The OOC innovation distinguishes are presented to the unfriendly responses of the medications and, at times, being lethal to them [77]. The OOC innovation identifies on the off chance that the various medications hurt liver cells. The procedure involves injecting the drug into various channels and seeding the chip with liver cells. based on Wikswo et al. If the chip is observed and the cells perish, the drug cannot be used in vivo [18]. The engineering behind liver-on-chips necessitates the integration of scaffolding materials for 3D cultures, cell growth, and maintaining cell interactions. These components, whether natural or manufactured, are utilized in numerous applications. Such applications might change from drug testing to conduct examination [77]. The majority of nanotoxicological effects-based liver-on-a-chip models are two-dimensional systems. One of the liver's most crucial functions is filtering and getting rid of toxins from the blood. One improvement to the

concept of a liver on a chip is the use of perfusions, which lengthens the cells' lifespan and improve drug metabolism [78].

5.2. Pancreas

Tumor of the pancreas has one of the worst prognoses because it has a high level of drug resistance and is challenging to surgically remove the tumor [79]. The unfortunate results of this illness are accepted to be brought about by the malignant growth cells which have high obtrusiveness highlights, consequently the disease arriving at cutting edge stages in a brief timeframe [80]. The pancreas's function is compromised by diabetes, a prevalent condition. The OOC is one tool that can be used to gain a deeper understanding of this condition. The scientists use OOC innovation to concentrate on the way of behaving of insulin creating cells to all the more likely grasp the peculiarity. It is normal that with assistance of OOC the endeavors of considering and understanding the infection ought to be sped up [81].

5.3. Brain

The brain might be the most intricate organ, and it is hard to create an OOC for it [82]. The models used in the majority of papers do not consider this issue because the functionality of the brain is far too complex and varies from person to person. Instead, they concentrate on cell ratios, the brain's transport capabilities, the neurovascular unit, and the blood–brain barrier. According to Wikswo et al., the ratio of neurons to glial cells varies depending on the brain section being studied [18]. In open environments like Petri dishes, in vitro cell cultures have been successful. Multistep lithography is the method that was used to culture the BOC. The soma and axon are separated in this procedure. This method allowed the examination, repair and treatment of axons by applying various drugs to them [83]. Established models focus on neurodegenerative diseases and are used to understand behavioral processes and their effects on synapses.

6. Future directions

OOC development receives favorable support from microfluidic chips. Its development has resulted in significant scientific advancements and has attracted international research attention. Numerous OOCs have been planned and constructed. Human organs of all kinds have been studied. The creation of a "Human on-a-chip" is the ultimate goal of OOC, which includes integrating multiple organs into a single chip and building a more mind-boggling multi-organ chip model. The human-on-a-chip theory is still a way off despite the rapid advancement of OOC technology. The most popular substance is PDMS, but it has some disadvantages because the final film is thicker than the in vivo morphology. The viability and poisonousness of soluble substances are impacted by a decreased absorbance of small hydrophobic particles. Recognizing reasonable elective materials is vital. As of now, the expense of assembling and trial execution is moderately costly, which isn't conductive to the inescapable utilization of organ chips, so parts should be of minimal expense and simple to arrange. More costly parts ought to be reusable. For widespread use, the media volume and connector size of integrated system components must be reduced. Because sample collection on the chip can interfere with its operation, changes in the concentration of different metabolites may take place. Better sensors are therefore necessary. It is also necessary to use general cell culture mediums that are appropriate for all organs. Most importantly, as the number of organs on the chip increases, functionality becomes more complex and generated data has a chance of being inaccurate and untranslatable. At this time, there is no way to fix this. The biomarkers identified in vitro may not exactly match those found in vivo due to long-haul rehashed organization or on-chip studies.

7. Conclusions

In drug development programs, drug discovery, harmfulness screening, and other areas, microfluidics and Organ-on-chip innovation have a wide range of applications. The incorporation of a fluidic system resembles the in vivo systemic response. The integration of multiple sensors makes it possible to monitor a variety of parameters in real time without harming the cells or tissues. The OOC idea has been around for quite a while

and has led to many new media breakthroughs. Given the complex interactions between different cell types in the environment, applications range from disease research to drug testing. OOC devices enable the creation of complex mobile microenvironments. For specific studies of many current interconnected OOC gadgets, some organ-on-chip models have been actively developed for almost all organs. One of the next steps is to integrate sensors into chips that facilitate compliance with critical physiological constraints. [84]. It is a significant field which with additional advancement can prompt new and progressive revelations. One of them is the human body embedded in a chip. In general, a specific organ may recover with the help of a medication used to treat a particular type of illness, but there are possible side effects that may affect other organs as well. Having a human body model that is made up of a configuration of OOC links could put an end to animal testing and speed up the pharmaceutical industry. New biomaterials and techniques that could make it easier to demonstrate some of the more difficult and mind-boggling physiological abilities. Numerous researchers have recently utilized the bioprinting concept, which may result in the OOC being produced at a lower cost. If bioprinting is used, it will save money, time, and money while also improving the design. More significantly, the various doors that are open can be used to automate medical procedures and end mistreatment. Due to its ability to mimic human organs or tissues, organ-on-a-chip technology has the potential to fundamentally advance the radiobiology field.

Declaration of Competing Interest

The authors declare that they have no known financial or non-financial competing interests in any material discussed in this paper.

Funding information

No funding was received from any financial organization to conduct this research.

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