Health Science
Communication

BBRC
Bioscience Biotechnology
Research Communications

Biosc.Biotech.Res.Comm. Vol 13 (3) July-Aug-Sep 2020 Pp-1218-1222

Applications of Microchip Based Technology in Modern Health Care: A Mini Review

Shubham Tyagi, Radhika Tyagi, Priya Chamoli, Neelam Negi and Amit Gupta*
[1]*Department of Biotechnology, Graphic Era Deemed to be University, Dehradun, Uttarakhand, India*

ABSTRACT

Human beings are mainly composed of different cells / tissues / organs which carry out various physiological roles representing a complex functional system. Now a days, it is difficult to predict the interactions between organs, including cells or tissues using in vitro cell culture approaches, as a result, animal tests should be conducted, pertaining to predict pharmacokinetics. So, major challenges as given through implantable technologies except the biomedical arena, showed some ignorance in mid-1990s. Few scientists have claimed some benefits about the usage of these medical-related technologies to patients, who have suffer from curable diseases or illnesses. Even today, scientists argue that this technology can be dangerous for the society at large, if applied incorrectly. Now, chip based technology has taken over the last few years. Various uses of microchips are applied especially in the field of medicine and human health care as well. The major benefits for this technology are reduced costs, low sample volumes, ease of use and precise results. This technology is to be used extensively in point-of-care diagnostics in less-developed countries. These chip based devices should be applied and are used to observe continuous or linked through various pharmacokinetics or immuno biological processes such as absorption, distribution, excretion, metabolism of various drug administration routes. Microchip technologies have all been expanded very rapidly and are coupled with various types of detection techniques which may be suitable especially for high-throughput screening including detection and mechanistic study of drugs. In this review article, we have discussed the importance and need of microchip technology for potential future development in the field of health care and diagnostics.

KEY WORDS: MICROCHIPS, TECHNOLOGY, MEDICAL SCIENCE HEALTH CARE.

INTRODUCTION

In spite of various new drug discoveries are reported but a major healthcare problem is still there because of non-existence of drugs for many infectious or non-infectious diseases. In addition, existing drugs are available somehow in the market but do not work in some patients and showed some side effects of drugs as well but considering as one of the leading causes of morbidity. Due to this reason, conventional studies were applied related to animal models for immunobiological research. In contrast, animal experimental based studies, raise some ethical issues and require new ways to improve drug development but their major drawback is the time-consuming process. Now a days, chip based technology is a recent contribution pertaining to solving various health care problems, especially in human systems, (mimicking

ARTICLE INFORMATION

*Corresponding Author: dr.amitgupta.bt@geu.ac.in
Received 14th July 2020 Accepted after revision 14th Sep 2020
Print ISSN: 0974-6455 Online ISSN: 2321-4007 CODEN: BBRCBA

Thomson Reuters ISI Web of Science Clarivate Analytics USA and Crossref Indexed Journal

Clarivate Analytics
crossref

NAAS Journal Score 2020 (4.31) SJIF: 2020 (7.728)

*Online Contents Available at: http//www.bbrc.in/
DOI: http://dx.doi.org/10.21786/bbrc/13.3/36*

human physiology with standard cell cultures on plastic substrates). Thus the existence of chips on organs which represent human tissues or cells of healthy individuals or patients under normal, or pathological conditions like those in the human body has been successfully developed (Kcomt 2019).

Healthcare is one of the most essential components related to human life. Now a days, number of chronic illness cases have increased enormously and have showed significant effects on modern healthcare (Kcomt, 2019). In spite of this, demand for researchers, doctors including paramedical staff members (nurses, microbiology and biotechnology) is extremely very high. In short, each country has its healthcare system, but there is some positivity and negativity as well (Borges et al., 2019). Those countries which are spending a lot of money on healthcare may have their other industrial sectors affected, while those countries which are spending less amount of money on the population's health, suffer more, (Lehnert et al, 2011; Gupta et al., 2018; Borges et al., 2019).As a result, this means healthcare can contribute more to the society which directly or indirectly is influencing human health. In short, healthcare arena is one of the most diversifying areas regarding preventive and personalized medicine (Guan, 2019). The measurement of health status is much more essential and advising patients including healthcare professionals on the most appropriate preventive, or curative measures (Hazarika, 2013; Borges et al., 2019; Guan, 2019).

In spite of this, our ability to evaluate our health status is totally hampered regarding complexity including cost, size and number of instrumentations that are required to acquire the data, and then analyze it. This type of data is much more required that transforms into more actionable information (Hazarika, 2013; Dikid et al., 2013). The major objective behind this technology is to improve its efficacy and morbidity using microchips where device manufacturers incorporate various technological advancements into medical implants. Recently, microchip based technology represents one of the new types of technological investmnents which is capable of drug release (on demand basis) over a long period, (Haitao et al, 2019; Kmiec et al., 2019).

The chip based technology has showed great potential and is more transformative related to modern healthcare systems. As per the literature, human studies involving microchips (e.g. dialysis) have been used and can be used in treating several other diseases such as diabetes and hypertension (Santini et al., 2000; Sharma et al., 2006; Rajgor et al., 2011; Haitao et al, 2019; Kmiec et al., 2019). In addition, microchips involvement is also seen to create artificial type of glands. The major role of hormonal regulation within the body which is directly associated with dysfunctional glands which helped in both controlling current disease state disorders and preventing them via other hormonal prompted disorders (Rajgor et al., 2011; Haitao et al, 2019; Kmiec et al., 2019).

The major challenge for biotechnological and pharmaceutical companies is regarding the testing of samples. In general, more than 92 percent of drugs undergo animal testing i.e. preclinical tests which is mandatory and required information but fail them to enter into the market (Akhtar, 2015). In an effort to reduce the budget cost, industries or institutes mostly relies on in vitro cell cultures and cell-based assays which is applied especially in biomedical research, pharmaceutical development and toxicity testing. In other words, in vitro cell culture is one of the most essential component of cell biology but its technology in advancement level may be declined as compared with the fields of genomics and proteomics and also through high-throughput testing of biochemical (Hartung, 2000; Coecke et al., 2005; Akhtar, 2015).

Scientists have developed some alternative methods regarding testing of animals pertaining to improve the assay validity and throughput capability is called organ-on-a-chip technology (3D human living cell cultures that are cultivated in a dynamic microchip environment under controlled condition that maintain human tissue functionality or mimic organ dysfunction). So, these disease-specific human cell types can be used to establish individual micro tissues with physiologic cellular behaviour, organ-on-a-chip technology can also be used for in vitro disease modelling (Hartung, 2000; Coecke et al., 2005; Akhtar, 2015). In this regard, device manufacturers incorporate some chemicals or drugs in microchips (solid silicon based) especially seen in medical implants (Haitao et al, 2019; Kmiec et al., 2019).

The designing of microchip is very simple and easy to manufacture but substrate contains multiple type of reservoirs which is capable of holding many chemicals in the form of solid, liquid, or gel form (Haitao et al, 2019; Kmiec et al., 2019). Overall, thus microchip is biocompatible and easy to implant in the human body. Each reservoir is mainly capped with a conductive membrane (i.e. gold) and wired with final circuit system which is controlled through microprocessor. In microchips, gold is used as standard membrane filter model because of its low reactivity with other substances, and also resists spontaneous corrosion in most of the solutions over the entire pH range. In addition, gold is considered as biocompatible material and presence of a small amount of chloride ion creates an electric potential region which favors the formation of soluble gold chloride complexes. In other words, this microchip may be considered as first device of its kind which enables the storage of compounds (one or more) inside the microchip in any form along with compound release on demanding basis, and with no moving parts (Haitao et al, 2019; Kmiec et al., 2019).

Background: History of microchips: is one of the most important parts of computer technology today and considered as a unit of packaged computer circuitry (also called as integrated circuit). This microchip is manufactured from one of the materials i.e. silicon at a very small scale.The process of creating a microchip

only begins with a type of sand called silica sand, which consists of silicon dioxide. In short, silicon may be the best candidate material for manufacturing process of semiconductor and always remain pure before used during manufacturing (Haitao et al, 2019; Kmiec et al., 2019).

- Introduction of first microchip in the year 1950s, but its size is much smaller as compared to fingernail and its cost so less than a dollar
- History of microchips started in the early 1950's when Geoffrey W. A. Dummer introduced type of software called them as microchips (immeasurable amounts of information and carry out various tasks, like today with I pods, computers, etc.).
- After 1958, researchers started making all sorts of sizes for microchip.
- In 1961, first commercially chips are available from Fairchild Semiconductor Incorporation. So, computers began to be made with microchips instead of individual transistors and their accompanying parts.
- In 1967, Jack Kilby invented the calculator (using microchips) and also won many awards including patents as well.
- Robert Noyce filed and published several patents and founded the company Intel, person is responsible for this invention i.e. microprocessor in 1968.
- In 1974, Roland Moreno from France who patented this technology called as smart cards or integrated circuit cards or embedded chip-on-a-card technology. This technology should easily identify the cardholder.
- In 1998, first demonstration of microchip implantation was achieved by Professor Kevin Warwick in case of human for identification and tracking purposes.

Chips are usually made in fabrication plants, multibillion-dollar investment and these are called as fabs. So, these fabs ultimately melt and refine sand to produce silicon ingots (99.9999% pure single-crystal). In addition, these saws slice the ingots and converted them into wafers (thick as a dime and several inches in diameter). Finally, wafers are cleaned and polished, and each one is used to build multiple chips (Chien et al., 2007; Morrison and Martin, 2007; Wu et al., 2015). Overall, all major steps are done especially in a clean rooms environment where precautions are taken pertaining to prevent contamination e.g. dust and other foreign substances. In addition, strategies are proposed with respect to human healthcare as shown in Table 1 (Chien et al., 2007; Morrison and Martin, 2007; Wu et al., 2015).

Table 1. Strategies for chip based technology and human health care

S.No.	Strategies
1	Design products, chip based which enable better clinical outcomes
2	This technology is applied in low-income based countries pertaining to reduce the program cost and implement its value of engineering to optimize product cost or development.
3	To build innovative ideas or solutions which may deliver high-quality, patient-centric care including improve access pertaining to advance diagnostics for millions of peoples.

Traditional methods for the fabrication of microchips:

- Photoresist- wafer, silicon dioxide, non-conducting layer is deposited on the surface and covered with photosensitive material called as photoresist. When photoresist is exposed with ultraviolet light which ultimately hardens that particular area exposed to the light (Faria-Briceno et al, 2019).
- Photolithography- Hardened process of photoresist called as photolithography, using different masks, followed by more etching and doping and repeated hundred times for the same chip and then finally converted into a more complex type of integrated circuit at each step (Basara et al., 2019).
- Each chip on the wafer is tested for correct performance, and then separated from other chips on the wafer by a saw. In view of this, good chips are placed in supporting packages that allow them to be plugged into circuit boards and bad chips are marked and discarded. In short, micro fabrication techniques (Heikkinen et al., 2019; Sen et al., 2019) have been contributed immensely to molecular technology, cell biology and medicine. The fabrication of a controlled drug delivery vehicle concerning architecture, topography, and functionality results in high predictability of in vitro and in vivo. So, these microchips represent as one of the most advanced fabricated well-developed technology and capable of releasing the drug over a longer period. The first microchip was developed in the year 1999 and this technology should be achieved already in vitro and in vivo with selected therapeutic agent along with regular pulses of drug expulsion into the experimental system (Haitao et al, 2019; Kmiec et al., 2019). Most of the therapies given to the patient which requires that particular type of drug should be repeatedly administered or in specific amounts at a time to maximize drug effectiveness (Haitao et al, 2019; Kmiec et al., 2019). However, various applications are applied in various, or different fields of medicine as shown below-
- This microchip based technique is applied in cancer therapy, especially for measuring the concentration of proteins within the blood (Hui et al., 2018; Yao et al., 2019). So doctors monitor the patients' health status especially in chronic diseases. Now a day, current methods for testing these blood proteins are too expensive and require too much blood to be performed regularly. In view of this, micro fluidic

chip is applied especially in clinical trials, and normally does on a single chip and results should come within 10 minutes. Similar types of results obtained by technician but it takes several hours to do this process only single drop of blood. So, this microchip based technology should give some hope and can be tried to use in diagnostic purpose. As per the literature, first development of microchip chip was reported by Caltech chemistry professors, James Heath and Leroy Hood, President and founder of the Institute for Systems Biology, in Seattle. Finally, Heath and Hood, formed a company called as Integrated Diagnostics pertaining to commercialize the blood chip (Irimia and Wang, 2018).

- This microchip based technology is applied in medical sciences, especially by doctors. These microchips are directly embedded in the patients body and doctors should monitor as well as control the drug release into their patients' body remotely through wireless connections, (Farra et al., 2012). One of the examples is seen in women where microchip drugs were given as hormones for bone strengthening, because they were suffering from osteoporosis and required daily injections of these hormones. According to the reports, this microchip was removed from the patient body after four months (Farra et al., 2012).
- Collaboration between Bio microelectromechanical Systems (BioMEMS) Resource Center and Massachusetts General Hospital (MGH) Cancer Centre has developed a microchip-based device pertaining to isolation, enumeration and analysing circulating tumor cells (CTCs; viable cells from solid tumors) from a blood sample. In this regard, CTC chip is prepared and showing some potential and considered them as valuable tool for monitoring as well as guiding the cancer treatment process (Haitao et al, 2019).
- The development of a microchip, especially for tuberculosis (TB) ELISA, is mainly responsible for detecting IgG responses against multiple type of antigens from plasma samples of active TB (ATB) patients in a rapid, and miniaturized detection system. This microchip utilizes Mycobacterium tuberculosis, surface glycolipid i.e. trehalose 6,6′-dimycolate (TDM) and two purified proteins, 38 kDa glycolipoprotein and antigen 85A (Ag85A), as antigens based on their known immunogenicity and their application in TB serodiagnosis (Gijs, 2004; Hua et al, 2019; Schneider et al., 2019).
- Both companies i.e. Massachusetts Institute of Technology, and Case Western Reserve University, developed microchip which holds measured doses of teriparatide (i.e. Forteo), injectable drug and is generally used to treat osteoporosis. This drug is difficult to administer but daily injections are required. In an effort to overcome this problem, chip (assembly consists of two chips on the surface of a titanium housing that holds the electronics) may be implanted in women who are suffering from osteoporosis but are healthy. As per the reports given by the doctors it was a surprise, that drugs dispensed through microchips showed more effective results as compared to those who had received ordinary injections as there was an increase in bone mass and mineral density as well but with no serious side effects (Gijs, 2004; Hua et al, 2019; Schneider et al., 2019).
- One of the approved FDA chips named as Verichip (now called Positive ID i.e. radio-frequency identification, RFID) started in the year 2004, allowed the physicians to easily access their patients, especially their health records. The size of the chip is equivalent to the size of a rice grain and actually can be implanted in the patient's arm. Instead, it contained a unique 16-digit identification number that would appear when the chip was scanned. With the help of microchip identification number, medical staff could easily access the patient's health records, (Gijs, 2004; Hua et al, 2019; Schneider et al., 2019).
- This chip technology is applied in diagnosis of various infectious diseases, especially detection of disease microorganisms (causing malaria, tuberculosis, diarrhoea, pertussis, and dengue); enteric infections (Escherichia coli O157:H7, Shigella dysenteriae, Salmonella, and Shiga Toxin-producing Escherichia coli). These organisms can be detected from a small amount of fecal sample on a microchip. In addition, microchips, awarded AAPS Drug Delivery Technology Award in the year 2008 for outstanding research in osteoporosis (Gijs, 2004; Hua et al, 2019; Schneider et al., 2019).

CONCLUSION

In medical science, chip based technology should transform or help conversion from unsustainable type of healthcare systems into more sustainable ones, which may equalize the relationship of medical professionals, doctors, scientists and patients. As this technology may provide cheaper, quicker and more effective means against various diseases it may help us win the battle for us against various dreadful pathogens. In short, microchip based technology is helpful in diagnosis as well as the screening of diseases, and also can be applied to other applications related to human health as well. Apart from these, this technology has played an important role in areas of drug discovery and delivery with respect to synthesis, screening of pure compounds, undergoing preclinical testing in vitro and in vivo. Recent developments and applications of microchip based devices have established fool proof research methods for analysing the effects of drugs at different time intervals as well. The ability of these microchips should be further used at the micro or nano level, which can be applied in high precision drug research including toxicity and pharmacokinetics.

REFERENCES

Akhtar A (2015) The flaws and human harms of animal experimentation, Special Section: Moving Forward in Animal Research Ethics. Cambridge Quarterly of Healthcare Ethics, 24, 407–419.

Basara G, Yue X, Zorlutuna P (2019) Dual crosslinked

Gelatin Methacryloyl hydrogels for Photolithography and 3D Printing. Gels, 5(3): 34.
Bohndiek SE, Brindle KM (2010) Imaging and "omic" methods for the molecular diagnosis of cancer. Expert review of molecular diagnostics, 10, 417–34.
Borges GA, Tortorella G, Rossini M, Staudacher AP (2019) Lean implementation in healthcare supply chain: a scoping review. J Health Organ Manag, 33(3):304-322
Chien CF, Chen HK, Wu JZ, Hu CH (2007) Constructing the OGE for promoting tool group productivity in semiconductor manufacturing. Int J Prod Res, 45, 509–524.
Coecke S, Balls M, Bowe G et al (2005) Guidance on Good Cell Culture Practice. A report of the Second ECVAM Task Force on Good Cell Culture Practice. ATLA, 33, 261-287.
Dikid T, Jain SK, Sharma A, Kumar A, Narain JP (2013) Emerging and re-emerging infections in India: An overview. Indian J Med Res, 138, 19–31.
Faria-Briceno JJ, Neumann A, Schunk PR, Brueck SRJ (2019) Measuring liquid drop properties on Nanoscale 1D Patterned Photoresist Structures. Sci Rep, 9(1), 5723.
Farra R, Sheppard NF, McCabe L, Neer RM, Anderson JM, Santini JT, Cima MJ, Langer R (2012) First-in-Human Testing of a Wirelessly Controlled Drug Delivery Microchip. Science Translational Medicine, 4 (122), 122.
Gijs MM (2004) Magnetic bead handling on-chip: new opportunities for analytical applications. Microfluid Nanofluid, 1, 22–40.
Guan J (2019) Artificial Intelligence in Healthcare and Medicine: Promises, Ethical Challenges and Governance. Chin Med Sci J, 34(2), 76-83.
Gupta S, Kapil S, Sharma M (2018) Improvement of laboratory turnaround time using lean methodology. Int J Health Care Qual Assur, 31(4), 295-308.
Haitao L, Yaqing W, Kangli C, Yaqiong G, Xu Z, Jianhua Q (2019) Advances in Hydrogels in Organoids and Organs-on-a-Chip. Adv Mater, 31(50), e1902042
Hazarika I (2013) Health workforce in India: Assessment of availability, production and distribution. WHO South East Asia J Public Health, 2, 106–12.
Hartung T, Gstraunthaler G, Balls M (2000) Bologna Statement on Good Cell Culture Practice (GCCP). ALTEX, 17, 38-39.
Haruyama T (2002) Micro- and Nanobiotechnology for Biosensing Cellular Responses. Advanced Drug Delivery Reviews, 1, 1-9.
Heikkinen JJ, Peltola E, Wester N, Koskinen J, Laurila T, Franssila S, Jokinen V (2019) Fabrication of Micro- and Nanopillars from Pyrolytic Carbon and Tetrahedral Amorphous Carbon. Micromachines (Basel), 10(8): 510.
Hua W, Zhan M, Juanxiu Q, Zhen S, Qian L, Xiaoyin C, Hengliang W, Zhenghua A, Wu L, Min L (2019) A versatile loop-mediated isothermal amplification microchip platform for Streptococcus pneumoniae and Mycoplasma pneumoniae testing at the point of care. Biosens Bioelectron, 1,126, 373-380.
Hui L, Su Y, Ye T, Liu Z, Tian Q, He C, Zhao Y, Chen P, Wang X, Han W, Luo Y, Wang B (2018) Self-Sterilizing and Regeneratable Microchip for the Precise Capture and Recovery of Viable Circulating Tumor Cells from Patients with Cancer. ACS Appl Mater Interfaces, 10(1):207-218.
Irimia D, Wang X (2018) Inflammation-on-a-Chip: Probing the Immune System Ex Vivo. Trends Biotechnol, 36(9), 923-937.
Kmiec MM, Tse D, Mast JM, Ahmad R, Kuppusamy P (2019) Implantable microchip containing oxygen-sensing paramagnetic crystals for long-term, repeated, and multisite in vivo oximetry. Biomed Microdevices, 21(3), 71.
Kcomt L (2019) Profound health-care discrimination experienced by transgender people: Rapid systematic review. Social Work in Health Care, 58 (2), 201-219
Lehnert T, Heider D, Leicht H, et al (2011) Review: health care utilization and costs of elderly persons with multiple chronic conditions. Med Care Res Rev, 68(4), 387–420.
Morrison JR, Martin DP (2007) Performance evaluation of photolithography cluster tools. OR Spectr, 29, 375–389.
Rajgor N, Patel M, Bhaskar VH (2011) Implantable drug delivery systems: an overview. Systematic Reviews in Pharmacy, 2(2), 91–95.
Santini JT, Richards AC, Scheidt RA, Cima MJ, Langer RS (2000). Microchip technology in drug delivery. Annals of Medicine, 32 (6), 377–379.
Schneider L, Blakely H, Tripathi A (2019) Mathematical model to reduce loop mediated isothermal amplification (LAMP) false-positive diagnosis. Electrophoresis, 40(20), 2706-2717.
Sen AK, Raj A, Banerjee U, Iqbal SKR (2019) Soft Lithography, Molding, and Micromachining Techniques for Polymer Micro Devices. Methods Mol Biol, 1906:13-54.
Sharma S, Nijdam AJ, Sinha PM et al (2006). Controlled-release microchips. Expert Opinion on Drug Delivery, 3(3), 379–394.
Wu NQ, Zhou M, Chu F, Mammar S (2015). Modelling, Analysis, Scheduling, and Control of Cluster Tools in Semiconductor Fabrication. Contemp Issues Syst Sci. Eng, 289–315.
Yao J, Chen J, Cao X, Dong H (2019) Combining 3D sidewall electrodes and contraction/expansion microstructures in microchip promotes isolation of cancer cells from red blood cells. Talanta, 196, 546-555