Abstract— The purpose of this paper is to document the technology trends in healthcare industry and predict future innovations and disruptions for entrepreneurial growth. We will overview the trends in point of care technologies, drug delivery systems and Organ-on-chip technology; evaluate market potential and the impact on health care industry in terms of cost and patient-physician relationship.

Index Terms—POC devices, drug delivery systems, organs-on-chips, market growth, impact.

Impact of Organ-on-chip technology on Drug Development process

I. INTRODUCTION

Over the next few sections we aim to provide a comprehensive view and estimate of how the technologies of point-of-care diagnostics, advanced drug delivery systems and organ-on-a-chip have evolved, where they are heading and what this means to entrepreneurs as well as people around the world.

Illustration 1: Health care industry

II. POINT OF CARE DIAGNOSTICS

Point-of-care is almost exactly as it sounds. Also known as near patient testing, POC testing can be defined as testing or human diagnosis done outside a traditional laboratory and near where the patient/test subject is.

As per BCC research, the global POC market has been steadily growing at an average CAGR of 4.5% since 2007 and is expected to reach at least 19 billion dollars by 2018. Illustration 2 is a plot of how the POC market has been trending.

Illustration 2: POC global revenue growth trend
Sources: BCC market research reports – HLC043B, HLC043C, HLC043D

Of the various segments in the POC market, the segment with the highest revenue is the glucose monitoring market with almost 7.5 billion dollars in revenue in 2013. This market is served by various glucose testing POC devices such as Telcare’s Wireless Glucose Meter, Bayer’s Contour Next Link and Sanofi’s iBGStar etc. These are not only compact devices but also equipped with cutting edge benefits like wireless communication, cloud storage and mobile device compatibility. Illustration 3 below shows how the point of care for diabetes testing has morphed over the years from a full sized lab to a simple i-phone compatible device.

Illustration 3: Evolution of point-of-care testing devices
Sources: BCC market research reports – HLC043B, HLC043C, HLC043D
Illustration 3: Labs are condensed to compact devices

Illustration 4 shows how the various markets within POC have trended over the years. You can note the promising growth in POC for infectious diseases and the cardiac marker markets.

Illustration 4: Growing market segments in the POC market

III. IMPACT AND FUTURE OF POC

The POC industry will most likely disruptively innovate and exponentially grow in coming years if not maintain its current growth rate. Below, we explore some of the prominent factors affecting the growth and future of POC:

1. Overall cost (money) – The total costs related to diagnostics and testing would be reduced due to lower turn-around time, lower waiting time, lower reagent and material costs etc.

2. Public health-care around the world (method) – The health-care systems for public would be more efficient and consistent which is a major requirement in many countries.

3. Shortage of man-power (men) – Recent trends in health-care workers and professionals project higher costs associated with manpower and lower returns. This can be overcome with simpler solutions like POC.

4. Technological advancement (machine) – A number of companies ranging from large establishments such as Roche and Johnson&Johnson to small startups such as Mbio diagnostics and SenGenix are developing new devices and platforms to make POC more prevalent and successful.

5. Trends in diseases and health related issues (Mother Nature) – Increase in the kinds of diseases, complications sprouting from health related practices are two primary drivers for POC innovation.

6. Globalization – With more connectivity, space and commercial opportunity worldwide more and more companies and startups are coming up with POC innovations and devices. The high awareness and drive would lead to better growth and development.

All these factors will be impacting the future of not just the POC markets but also the number of new startups, entrepreneurial ventures, investment and innovation. Given below is a distribution of the POC market globally. The total market is divided geographically as North America, Europe, Asia and the rest of the world. The size of each bubble represents the estimated proportion of population in that region, the vertical (Y) axis is percentage of the global POC market.

What we can clearly see from the plot is that though Asia is much higher in population and POC demand, there is only 14% of the market share there. North America, as the least populated geographical region has more than 50% of the market share. The rest of the world which includes key regions such as South America, Africa and Australia etc. is a meager 3.5%.

This plot allows us to infer the following:
- The global POC market is bound to grow and expand to meet the demand in areas such as Asia
- While expanding to areas like the Africa and Asia, cost becomes a crucial factor in diagnostics and this would lead to inevitable disruptive innovation in the POC device market - The WHO estimates that around 100 million people enter the poverty zone every year because they had to pay for their medical bills
- Technological innovation and disruption would lead to more compact, inexpensive, readily available devices which will also impact the first world economies like North America and Europe
➤ There is and will be more opportunity, encouragement and investment in global POC related businesses and ventures – innovative ventures are constantly coming up like Biosensia, Radisens Diagnostics, Google lens for glucose measurement and so on
➤ Specific POC devices will gain markets considering the top causes of death and ill health – cardiovascular diseases, infectious diseases and cancers

IV. ADVANCED DRUG DELIVERY

Until recently, drug delivery has been mostly limited to orally consumable pills and syringes, which leads dose peaks at the time of administration. However, recent research and advances indicates toward alternatives that not only provide sustained and controlled drug delivery but can also target specific organs in the body. This will have a substantial positive impact on the drug potency and will most definitely reduce the side effects attached to modern drugs. Additionally, the risk attached with needle-based delivery systems such as possibility of HIV, Hepatitis B and Hepatitis C infections has highlighted the need for alternate and more effective methods. There is also a need for delivery methods that accentuate the life of unstable drugs and make them available in the underdeveloped regions of the world. Lastly, the drug delivery industry is yet to catch up with the advances in the smartphones and reap the benefits in patient care that could be achieved by collaborations between the two industries.

V. HISTORY OF DRUG DELIVERY

Historically, the most common form of medication has been an orally administered pill. Refer to Illustration 6 for a sample development of drug delivery. Around 500 B.C, shaped clay lozenges were proscribed for a variety of conditions on Mediterranean island of Lemnos. A major breakthrough in drug delivery mechanisms came in the mid-nineteenth century when Edinburgh physician, Alexander Wood published a paper on subcutaneous injections and British inventor William Brockedon received a patent for manufacturing pills on an industrial scale. By 1950’s, the first controlled release drug, Nitroglynn was introduced in the market. It used multiple coatings on drug pellets placed in a capsule that dissolved at different rates, keeping the concentration of drug in body for a longer duration. Tiny lipid bubbles called liposomes were first proposed as drug carriers in 1972. In 1976, Robert Langer and Judah Folkman made a groundbreaking discovery and showed that large molecules could be delivered over days and weeks from polymer matrices, and the release profile could be tailored based on the matrix. The first birth-control device Norplant was introduced in 1991. Once implanted under the skin, it consists of six silicone rubber tubes that release a continuous dose of the hormone levonorgestrel. In, 2003, the first coronary stent was approved by the FDA, which slowly releases a medication to keep coronary arteries open after angioplasty. The next set of devices that we expect to see in the market will revolutionize the drug delivery market. They include but are not limited to programmable implants for sustained and targeted drug delivery, sensor controlled patches and ocular devices for needle free delivery. The next challenge for researchers is to solve interdisciplinary challenges involving highly complex biological systems within human body.

Classification of drug delivery – Technology

1. Sustained release drug delivery: With the limited success and high cost attached to drug research, it becomes imperative that maximum benefit be derived from existing drugs. Sustained release mechanisms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. Illustration 7 shows the advantages of using sustained delivery with existing drugs. Sustained delivery is among the most researched area and many oral, implant and transdermal systems are available in the market for immediate use. Based on BCC Market research data, Sustained drug delivery systems had 13% market share among all drug delivery technologies. Sustained drug delivery technology can further be divided into oral and micro-syringes based systems.
2. **Prodrugs**: A drug that is first administered in an inactive form, which then becomes active through interaction with metabolic processes of the body, can be classified as a prodrug. They are used to predominantly improve absorption and distribution of drugs that show poor absorption through the gastrointestinal tract. They are especially useful in treatments with possibility of adverse or unintended effects such as chemotherapy. In 2003, Testa and Mayer discovered that Aspirin is rapidly hydrolyzed in the intestinal wall and liver, as well as in the blood to salicylic acid making it a valuable prodrug. Based on BCC Market research data, Prodrugs had 10% market share among all drug delivery technologies.

3. **Implant and intrauterine devices (IUDs)**: An implant is a foreign object inserted in the body. The most commercialized application of this technology is birth control and IUDs are among the most effective form of long-acting reversible contraception.

4. **Targeted drug delivery**: Targeted drug delivery works on the principle of targeting specific tissues of interest while reducing relative concentration of the drug in other regions of the body. It is also sometimes known as smart drug delivery. Cancer drugs serve as the best example due to their inherent toxicity and need targeted drug delivery inside the human body. Targeted drug delivery use vehicles, which are nontoxic, biocompatible, and biodegradable and avoid recognition by the host’s defense mechanism. This delivery mechanism has the highest market share of about 54% of all drug delivery systems.

5. **Polymeric drug delivery**: Drugs can be embedded or conjugated in polymer matrices which act as a controlled-release systems providing constant doses over long periods, cyclic doses, and tunable release of both hydrophobic and hydrophilic drugs. Polymeric drug delivery devices can further be categorized as diffusion-controlled, solvent-activated, chemically controlled or externally triggered systems.

Drug delivery systems can also be categorized as oral, injectable, pulmonary, nasal, oral mucosal, rectal, ocular and transdermal based on the route of administration.

**VII. Market Assessment**

Effective delivery mechanism plays an important role in the commercial success of any drug. Based on BCC market research report, drug delivery sales rose from $166.6 billion to $176.7 billion between 2011 and 2013. The market is expected to grow at a CAGR of 4.2% and cross the $210 billion mark by 2018. This industry face major challenges in terms of uncertainty related FDA approvals, patent disputes and competition from generic products.

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<th>SkysPharma, Direct, Bend Research, Therakine, ddi</th>
<th>Incube Labs, SurModics, Endocyte, Akrivis, Medimeetrics</th>
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<td>Injectable</td>
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<td>Direct</td>
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<td>Invasive</td>
<td>Microchips</td>
<td>Microchips, Incube Labs, Biosensors, Medronic</td>
<td>Heran Therapeutics, InnoCore</td>
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<td>Direct, Zosano, Aveva, LTS</td>
<td>Vaaxas</td>
<td>Targeted, Polymeric</td>
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Illustration 8: shows a list of dominant and emerging drug delivery companies.

**VIII. Technology Trends**

There is distinct need to overcome the reduction in profits related to the discovery of new drug because of the uncertainty in the approval process. Drug delivery systems provide a dual benefit of improved patient care and an alternate source of revenue for pharmaceutical companies. The next wave of drug delivery devices is expected to be a smart amalgamation of latest sensor technology and existing devices. Google filed for a patent for ‘smart’ contact lenses, which would help people with diabetes, monitor their blood sugar. Personal healthcare and disease management with wearable sensor-laden devices that provide continuous measurement of key physiological parameters, coupled with data storage and drug delivery will transform the lifestyle of patients. The 25.8 million Americans suffering from Diabetes will no longer need to regularly monitor blood glucose or use syringes to administer insulin. It is expected that these advances will significantly reduce the cost of diagnosed diabetes, which is around $245 billion per
year. Microchips’, a start up by industry pioneer Robert Langdon, is building programmable drug delivery implants that hermetically seals discrete doses of drug in each micro-reservoir, and releasing that drug on schedule or demand. Microchips technology has the potential to significantly reduce the pain attached with the treatment, ensure patient compliance better quality of life. Another area of considerable research is wearable patch technology that could deliver large molecules like proteins and peptides, thereby completely eliminating the need for syringes. A lot of emphasis is currently being spent on the research of biodegradable polymers and ceramic implants that could revolutionize the way we administer medication today.

IX. ORGAN ON A CHIP

The pharmaceutical companies in the United States spent a massive $50 Billion on developing drugs in 2013. The number of drugs that hit the market was a mere 27. On an average, it costs close to $1.2 Billion to discover and develop a drug. This is ten times of what it used to be 5 decades back. If this trend continues, pharmaceutical companies may not bear these unrealistic costs. This paper talks about how the present drug delivery process might be disrupted by the introduction of Organ-on-a-chip technology.

Let us first briefly understand what an Organ-on-a-chip does. After a good breakthrough in Lab-on-chip technology, researchers have started working on a technology called Organ-on-chip. An Organ-on-a-Chip is a multi-channel 3-D microfluidic cell culture chip that simulates the activities, mechanics and physiological response of entire organs and organ systems. They are the result of combining Lab-on-a-chip technology and 3-D cell culture models.

Organ-on-a-chip mimics the structure and functions of a living human organ on a clear, flexible microchip. They are subjected to actual physiological conditions that take place inside the human body. This microchip response to infection, inflammation, environmental toxins, and drug delivered to the chip.

X. CURRENT DRUG DEVELOPMENT PROCESS

Let us look at the current drug delivery process (Illustration 9) followed in the healthcare industry. On a broader level, it consists of five stages as shown in the figure below.

Illustration 9: Current drug development process

More than 5000 drugs are discovered at the beginning stage, which filters down to approximately 250, in the preclinical research step. After being tested in labs and on lab animals, the number shrinks to 5 when the process reaches clinical trials. A single drug is finally approved by the FDA after passing through 3 phases of testing on humans. The entire process takes 10 to 12 years with a whopping expenditure of $1.2 to 1.3 billion.

XI. IMPACT OF ORGAN-ON-A-CHIP

The current model for drug discovery and development is ineffective, and in recent years, increased financial stress, dwindling pipelines, and persistent failures in the clinic have created a critical need for better and more predictive research tools for drug discovery applications.

According to Wyss Institute at Harvard University, Organ-on-a-chip will, one day, eliminate preclinical trials. The testing on thousands of animals can be avoided if this technology can produce the same or even higher quality analysis.

The major inefficient stages in the drug development process are Preclinical trials and Clinical trials. Around 75% of total drug development cost is consumed in these stages. If we look at preclinical trials, the success rate of a drug making it through this process is just 34%. The cost incurred in this stage is around 22% of the total drug development cost. The number of animals used for testing is high, approximately 150,000 animals in a year, which are subjected to painful procedure. Since organ-on-a-chip mimics a living organ, it can avoid the need for using lab animals and in turn provide a cost effective alternative with higher accuracy.

If we look at Clinical trials, the success rates are around 60% for Phases I and III and 30% for Phase II. But the cost incurred is almost half (57%) of the total cost of the development process. Even if some part of this is replaced by organ-on-a-chip, the cost reductions will be significant.

Let us look at the impact of Organ-on-chip stage wise:
Projected cost of drug development in 2030 based on the current trend (Illustration 10):

![Illustration 10: Expected cost of drug development](image)

The cost of developing a drug will reach approximately $2 Billion in the coming decade based on the present trend. The forecast has been predicted linearly based on data collected from the year 1970 to the year 2012. If organ-on-chip replaces preclinical trials, we can expect the costs to go down as shown below in Illustration 11:

![Illustration 11: Expected cost of drug R&D if preclinical research is replaced by Organs on chips](image)

Illustration 11: Expected cost of drug R&D if preclinical research is replaced by Organs on chips

Although the cost reduction is not significant, the impact on reducing number of lab animals is significant. If we look at the trend with respect to use of lab animals during the past, Organs-on-chips will help research labs to save thousands of animals. The objective of testing drugs in animals is to find out the implications of the drug on humans. But various research papers suggest that the correlation between effects of drug on animals and humans is very low. This is one of the reasons why drugs fail during Phase I of Clinical trials. Organs on chips can be very beneficial in increasing the accuracy since they will be replicating the exact metabolism of a human organ. If organ-on-a-chip replaces both preclinical trials and some part of clinical trials, potential savings in R&D cost of drugs would be as shown below. Illustration 12 is based on the assumption that each phase is eliminated by Organs-on-chips every five years.

![Illustration 12: Expected drug R&D cost if preclinical and clinical research are replaced by organs on chips](image)

Illustration 12: Expected drug R&D cost if preclinical and clinical research are replaced by organs on chips

Since this technology is not yet out commercially, it is hard to tell its exact implication. According to the researchers, it is bound to reduce the cost of drug development process, the duration of some of the stages it eliminates and help speed up the process.

**XII. CONCLUSION**

So the POC market is one of the levers to improve health-care globally and it is destined to grow and disruptively innovate. The market needs globally are growing in continents like Africa, Asia and South America where there is a lot of opportunity.

Illustration 13 is a look at the trend of health-care and social assistance establishments. We can see a gradual drop in these establishments and a shift happening towards point-of-care and mobile applications more aggressively.

![Illustration 13: Trend of health care establishment startups](image)

Illustration 13: Trend of health care establishment startups
An excellent technological segment of POC is m-Health or mobile health. This segment is driven by mobile platforms and devices using applications that perform point-of-care diagnostics for users with mobile devices. China, India and Africa are three major regions with more need for POC and more mobile devices being used than USA or UK. Below is Illustration 14 with a trend of the m-Health market in North America, Europe and Asia Pacific as estimated by BCC market research report HLC162A.

Illustration 14: mobile healthcare trends in North America, Europe and Asia Pacific

With these exponential prospects and opportunities, we will soon be part of an efficient world where no one compromises health for time or money or lack of awareness. The common man would be able to affordably diagnose and keep check of his health and consult doctors both physically and remotely!

Historically, drug delivery device and drug development worlds have been separate, with only a handful of companies having a successful and substantial track record in both. Though there is a genuine need for the convergence of the drug discovery and the device industry, yet there is limited coherence between the two. Different skill sets, regulatory and compliance processes, infrastructure and development cost has restricted this partnership to limited companies. To extract the full commercial value from the device element, the business case and high level product requirements for the drug/device combination must be developed when the drug is in early development. However, the uncertainty related to the success of the drug discovery process, the high cost and regulatory hurdles make early decisions for collaboration a difficult choice.

The current drug development process has been around for decades, with costs rising every year at unprecedented rate. The process is time consuming with low success rate. It still relies on experimenting on animals to study the implications of the drug on Humans. Organs on chips can be that disruptive technology which will help eliminate the need for animals and test the drugs directly on artificial human organs. Body on chip, which is an integration of all organs on chips, can act as an actual human, upon which drugs can be tested more comprehensively. The day is not far when our cells are taken to lab and drugs are customized based on our individual needs.


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