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Master Degree Project in Innovation and Industrial Management

Bringing 3D Bioprinting to the Market

Agile marketing, rapid product development and strategic alliances

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Master's Thesis in Innovation and Industrial Management

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ABSTRACT

3D bioprinting technology is an emerging technology with a potential to revolutionize the medical field as it has a capability to biofabricate living tissue and organs using a patient's own cells in conjunction with different biomaterials. This disruptive technology is in an early stage and innovators and early adopters stepwise improve the performance of the technology as it continuously grow. The first official 3D bioprinting company, Organovo from the USA, found their niche market in providing pharmaceutical companies with human tissue on demand that can be used for drug screening applications.

This thesis describes a novel model used for bringing 3D bioprinting to the market, disrupting the current market established by Organovo. CELLINK AB, which is the first company in the world to commercialize a universal bioink for bioprinting of human tissue, has realized that successful commercialization stems from the creation of a system of products, rather than single products. Such system includes the commercialization of 3D Bioprinters, bioinks, consumables, and even bioprinting services for educational use. Providing bioprinters and bioink require, however, that the demand for such goods and services grows simultaneously. The strategic alliances with material suppliers and partnership with cell supplier played an important role in paving the path to market for CELLINK. The missing link, such as lack of CAD files of human tissue and organs, has been filled by creating an open source community, namely "Bioverse". CELLINK, a start-up company found their niche by becoming the first 3D bioprinting company in the word that provides the whole introduction package to 3D bioprinting for innovators and early adopters. Agile marketing, rapid product development and strategic alliances were keys to CELLINK's success. CELLINK is currently positioned in a rapid expansion stage and must focus heavily on R&D, sales and marketing to maintain its market shares and continue the growth. The following case study is an analysis using the Knowledge Intensive Entrepreneurship, KIE conceptual model (McKelvey, Lassen, 2013).

Keywords: *3D Bioprinting, CELLINK, Agile Marketing, Strategic Alliances, Disruptive Technology*

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Firstly, it has been a true pleasure to partake in the Class of 2016 Master's of Innovation and Industrial Management at the Gothenburg University. My time at the University has been beneficial for both my professional career as well as my personal life and I have a plethora of great memories that I will bring with me throughout my life. With that, I would sincerely like to show my gratitude and appreciation to Professor Maureen McKelvey for providing me with a great education and challenge me intellectually throughout my time at Gothenburg University. I also want to thank the rest of the faculty at Gothenburg University for the education as well and their time and efforts. My time at Gothenburg University has been a true pleasure thanks to this.

Lastly, I would like to show my sincere appreciation to my supervisor Evangelos Bourelos for his time, understanding, and for not giving up on me. He has truly been a great support to me throughout the entire education.

Gothenburg, October 26th

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Erik Gatenholm

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1 INTRODUCTION

This section gives an introduction to the company CELLINK and presented the relevance in this thesis followed by the thesis purpose and limitation.

1.1 BACKGROUND

CELLINK was started as a joint European Eurostar project between the four partners; two from the industry and two from academia. The purpose of the project was to develop a universal bioink with the ability to successfully grow human tissue in vitro. The deliverables set within the project were narrowed down to the successful growth of two types of soft tissues; skin and cartilage tissue. All partners possessed the high-end competencies and also capabilities to deliver results, and the cooperation was regulated by the signed partnership agreement to further ensure performance guidelines and deadlines were followed. The contributions by the partners brought in a unique mix of prototypes that have further been developed into products. During the project, several discoveries have been made in regards to the current gap on the 3D bioprinting market and the growing demand for entry level start packages consisting a sophisticated, yet affordable 3D bioprinters, standardized bioinks for tissue growth, consumables and protocols that allow customers to perform successful bioprinting.

Such package was successfully introduced to the market by CELLINK through direct marketing channels such as exhibitions, trade shows, conferences and but also through the creation of websites and webshops, and marketing through social media channels such as Twitter, Facebook, Instagram, and YouTube.

CELLINK was started as a project and an intraventure within a consulting company and became a stand-alone company through a spinoff process. Within very short time, the company became unique a 3D bioprinting company with great potential for further growth.

The future development and success for CELLINK as a company requires reinforcements of several areas, such as marketing, product development, manufacturing, and post market activities. The current focus is on sales and deliveries, as should be for a small startup. Customer closeness is, however, one of the most important success factors and require additional attention to ensure not only continuous use of the company's 3D bioprinter, but also adoption of the business model of selling a bioprinter cost effectively and then continuous sales of bioinks. This report is meant to summarize the current status and provide

suggestions for the company's long-term roadmap. It will also include some ideas for the establishment of long-term strategic alliances.

CELLINK has been evolving rapidly from the CELLINK project, with the title: "Biofabrication of 3D soft tissue models with a tissue-printing technology and a biosynthetic nanocellulose". The project outcome is a developed technology platform to biofabricate (bioprint) 3D soft tissues, such as skin and cartilage, with a defined microarchitecture and structural integrity using nanocellulose from wood as a cell compatible, injectable scaffold/bioink.

The original aim of the EUREKA/EUROSTAR project was to develop a technology platform that would enable the biofabrication of 3D living human tissues in vitro, "tissue-on-a-plate", stable for time periods ranging from a few weeks to several months. The project focus was on the biofabrication of soft tissues using a new generation of 3D bioprinters and a nanocellulose material as an injectable scaffold/bioink. The first aim of the project was bioprinting of skin tissues, which is highly desired by the cosmetic industry as a model for the evaluation of new cosmetic products instead of using animals; and cartilage tissue, which is of interest as an osteoarthritis disease model and also for translation of stem cell technologies for reconstructive surgery in the field of cartilage repair.

Successful R&D work has resulted in the development and optimization of a nanocellulose based bioink with unique printing fidelity and an excellent cell biocompatibility. This novel bioink, the first product offered by CELLINK, was introduced to the market as the first universal bioink in the world for 3D Bioprinting of human tissues and organs. However, upon commercialization, and even though immediate market response, the team realized that the market for bioinks is very limited due to the lack of bioprinters on the market. The lack of bioprinters stemmed from the fact that such technology was still very expensive and only a few companies in the world manufactured them. There were already cost effective ones available, however, their business model was not involving any bioinks as this was outside their expertise. The CELLINK therefore decided to develop their own 3D Bioprinter and executed this process in only four months. Such rapid development and commercialization is unheard of within the biotech industry.

The new strategic development changed the market introduction approach from solely selling the bioinks to offering a complete starting package for beginners in 3D Bioprinting. The package was met by a great market response, which resulted in immediate sales. The original concept of selling just bioink was changed to marketing and sales of a system

consisting of several components, such as: a 3D bioprinter (INKREDIBLE), a device developed to mix human cells together with bioinks and biomaterials (CELLMIXER) and the CELLINK Bioink. In addition, a strategic alliance with the U.S. stem cell company RoosterBio Inc, was formed in conjunction with the launch of the 3D bioprinter and together both companies offered the first "Ready to Print" cell/bioink package, which provides a unique functionality to grow human skin- and cartilage tissue (2).

1.2 PURPOSE

This thesis investigates a novel model for bringing a disruptive technology to market for a specific company, CELLINK.

1.3 LIMITATIONS

In this report the time frame has been narrowed down to the point when CELLINK has been established on the market as one of the top 10 bioprinting companies worldwide. I have also used fictive names to describe some of the partners, suppliers and customers since CELLINK is a company and cannot fully disclose such information.

Since the field of 3D bioprinting is under the rapid development, some of the data may not be valid any longer.

1.4 THESIS OUTLINE

Chapter 1 – Introduction: An introduction of the thesis is presented to provide a motivation and short preview of the thesis. A background description of the case company as well as the purpose followed by the scope is presented

Chapter 2 – Methodology: The study design and what research approach has been utilized is described followed by information on how the literature research and data collection has been performed.

Chapter 3 – Theoretical Framework: The relevant theories and models used in this thesis are here presented. Furthermore, the case company is presented in detail.

Chapter 4 – Case Company - CELLINK: Deep diving into the company CELLINK and its characteristics.

Chapter 5 – Analysis and Discussion: The analysis and discussion is based on the precious findings in the theoretical framework as well as empirical findings from the case company.

Chapter 6 – Conclusion: The answer to the purpose of this thesis is here presented followed by the relevance of the thesis and future research suggestions.

2 METHODOLOGY

In this chapter, the research design of the study and a description of what methods that have been used to retract data are presented as followed. The design of the study as well as what research approach that has been utilized is firstly presented followed by information on how the literature review and the case study has been performed.

Figure 1 shows an overview of how the work has progressed from problem and purpose definition to a final conclusion. The whole process has been iterative based on information gathered throughout the period and purpose and problem definition has been redefined as new interesting fields have been introduced. Finally, the results have been combined and discussed, in order to establish a conclusion.

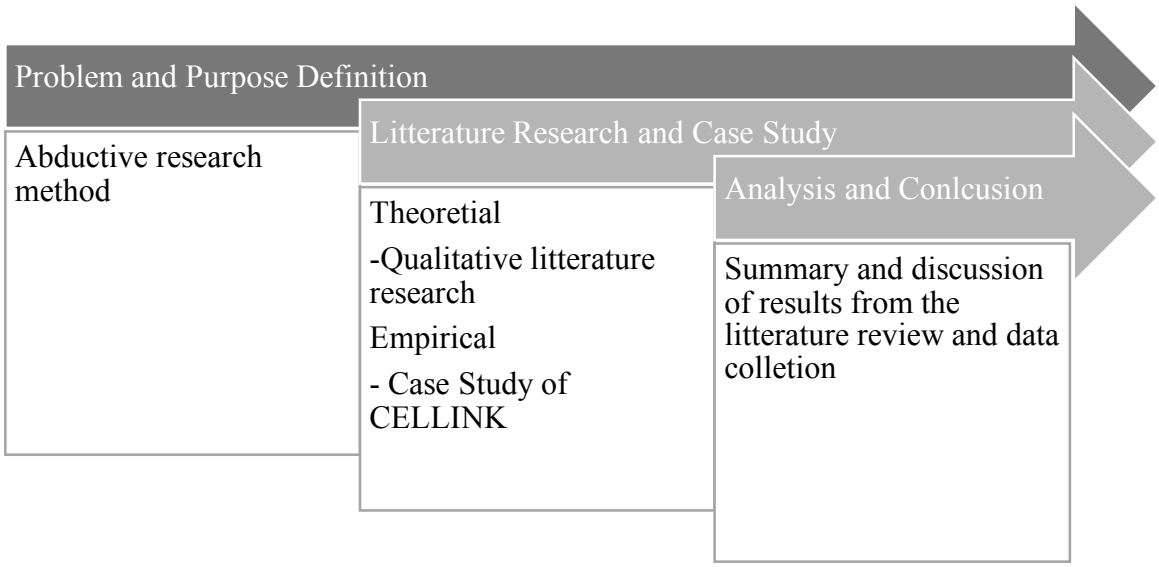


Figure 1 - Terminology of the thesis process

2.1 RESEARCH APPROACH

The research in this thesis consist of two blocks, one empirical and one theoretical. The empirical block is based on a case study of the company CELLINK, while the theoretical block is based upon a literature review. The thesis itself was based on a combination of a hypothesis deducting method and an inductive method namely; an abductive method approach (Wallén, 1996). The idea behind this approach is that neither a theory nor empirical findings should stand alone, instead, by iterating between the two, a researcher can draw a

more accurate conclusion based on both theoretical and empirical phenomena. (Dubios and Gadde, 2002).

Furthermore, this approach allows the researcher to re-modify the original framework as new interesting fields are investigated. Hence, the thesis can be considered as more flexible approach since new theories may change the author's initial ideas, and should so be able to. For this thesis, the method is suitable as it is built upon an empirical case study and a qualitative literature review that both have significant value to the final conclusions. In addition, the method does not require an initial hypothesis which, in this case an initial hypothesis is considered to eliminate possible solutions.

To properly address the purpose of this thesis, a case study of the specific company, CELLINK, was considered as the best solution. Hence, the foundation of the thesis was based upon a qualitative single-case study of the company CELLINK in order to find a novel model for bringing a disruptive technology to market. A qualitative approach in this case refers to an in-depth analysis of a single company. The idea is to, by combining a qualitative literature review and a case study, understand how a company successfully can bring a disruptive technology to the market. According to Yin (2003), a case study should be used for researches when the question is based on the wording "how", The case-company CELLINK was chosen in order to better understand its specific needs as it was of special interest for the author.

A case study enables the researcher to closely examine data in a specific desirable context in order to draw general conclusions. In this case, the method is used more specifically to draw conclusion on the case-company and not to create a generic model for all companies within the field of a disruptive technology. Nevertheless, conclusions drawn in this thesis may be beneficial for companies within likewise context (ibid.).

One of the common pitfalls associated with a case study is to not consider proper limitations. Authors generally have the tendency to answer questions that are too broad. Several authors including Yin (2003), and Stake (1995) suggest some guidelines to prevent this phenomenon. They suggest that the case should be limited by time and place, time and activity, and by definition and context. By answering upon these questions, the study remains within a reasonable scope. This study was performed between February and August 2016 in Gothenburg, the activity was based on gathering information about company specific details that could be of use to the analysis and, the context is to understand how CELLINK in particular can bring their disruptive technology to the market.

For this thesis, an intrinsic case study was chosen. Stake (1995) argues that this study is best performed when the researcher has a genuine interest in the case and where there are no expectations for the results to have implications for other case studies. This thesis focus primarily on CELLINK as a company with its specifications and no generic conclusions should be drawn. The company itself is also of genuine interest to the author and conclusions drawn in this thesis can and most probably will be used for CELLINK.

2.2 DATA COLLECTION

Data in this thesis was collected in two ways, one literature review and one case study of a company. The two methods are presented in this chapter.

2.2.1 Literature review

A literature review is considered to be a powerful tool when performed a research within a specific field (Bryman and Bell, 2011). It works as a great support for this thesis as limited time and resources makes it impossible for the author to investigate all the areas included in the analysis and conclusion. Furthermore, using published researches, also known as secondary data, should be considered as a more reliable source than self-conducted unverified research. Hence, the main reason for this literature review was to gain knowledge from already established theories within the field.

The amount of information available is extensive and in order to find accurate data for the thesis, and initial screening of what is there was conducted. The aim here was to collect secondary data originating from articles and reports made by other researchers to gather information on the bioprinting market, competitors to CELLINK, knowledge intensive entrepreneurship and the disruptive market. The data was extracted from relaible sources such as published articles, well-known webpages within the industry and books.

2.2.2 Empirical Case Study

Data collection in regarding the case company CELLINK was made by a case study as earlier mentioned. Data was extracted both from internal company specific documentations, articles made on the company as well as personal insights since the author is the owner of the company.

3 THEORETICAL FRAMEWORK

In order to reach an understanding of how CELLINK has brought its product to the market and to be able to analyze the findings and draw conclusions, relevant theories and models have been studied. This chapter contains information regarding the 3D bioprinting industry, company specific details concerning CELLINK and models to bring a product to the market.

3.1 DISRUPTIVE TECHNOLOGIES

The term "disruptive technology" was coined by Clayton M Christensen (1997) and refers to a new technology having lower cost and performance measured by traditional criteria, but having higher ancillary performance. Christensen (1997) finds that disruptive technologies may enter and expand emerging market niches, improving with time, and ultimately attacking established products in their traditional markets.

According to Christensen's (1997) theory of disruptive technology, the establishment of a new market segment acts to channel the new product to the leading edge of the market or the early adopters. Once the innovation reaches the early to late majority of users it begins to compete with the established product or products in its traditional market. An alternative scenario is that a higher performing and higher priced innovation is introduced into the most demanding established market segments and later moves towards the mass market (Christensen, et al., 2004; Walsh, 2002).

3.2 KNOWLEDGE INTENSIVE ENTREPRENEURSHIP (KIE)

Knowledge Intensive Entrepreneurship refers to the phenomenon of startups and entrepreneurial companies being mainly created on the basis of different types of knowledge. Further, this knowledge base is divided into three main areas, namely: scientific and technical, market and end-user, and organizational management. These three knowledge areas are essential for the creation of a technology company and in CELLINK's case, these three knowledge areas have been present and vital for the development and commercialization of the company's technology. In addition to the three main area, there are other areas that play a significant role on the development of a Knowledge Intensive Entrepreneurial firm, such as the ability to access different so called inputs. These inputs, as described by Lassen and McKelvey (2013) and are presented in the KIE Creation Model mainly refers to the:

- Sources of Knowledge
- Characteristics of the founders
- Financials

- Society and its effects on the venture

Further, this case study will focus on high-tech entrepreneurial ventures where there is significant innovativeness in the product or technology area as well as where the technology is based on scientific findings and academic education (Lassen & McKelvey 2013). Figure 2 illustrates knowledge intensive entrepreneurship, the KIE conceptual model (How entrepreneurs do what they do, Edited by M. McKelvey and A. Heideemann Lassen, 2013

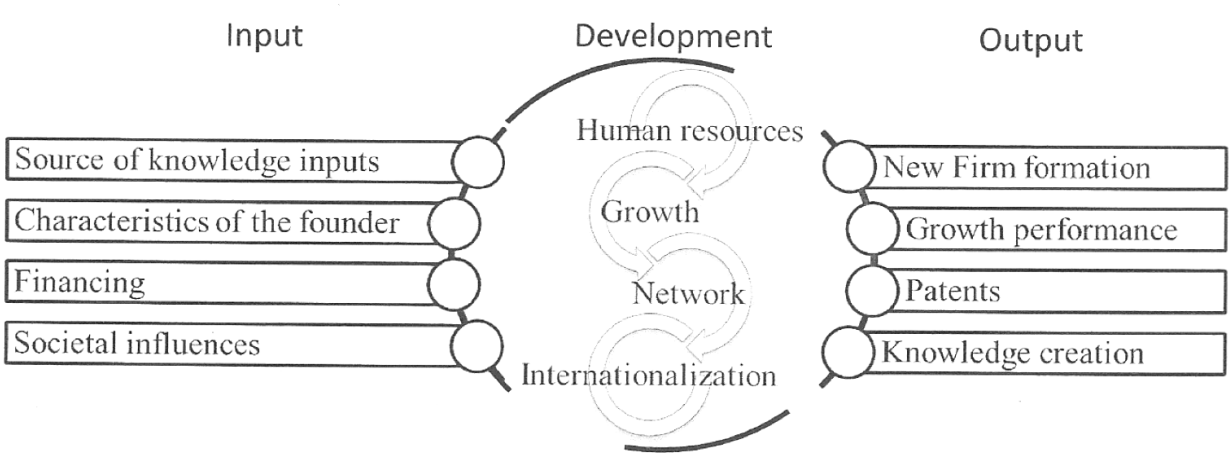


Figure 2 - Knowledge Intensive Entrepreneurship, KIE conceptual model (How entrepreneurs do what they do, Edited by McKelvey Lassen, 2013)

The model is based on intensive knowledge inputs, and characteristics of the founders.

3.3 SCAFFOLDS FOR TISSUE ENGINEERING - TECHNOLOGICAL ALTERNATIVES

Tissue engineering is an emerging, multidisciplinary field involving cell biology, material science engineering, and mechanical engineering to fabricate biological constructs that will restore, maintain or enhance normal function in diseased and injured tissues (Griffith, 2002). One of the primary conclusions from the past years in tissue engineering and stem cell therapy is that conventional two-dimensional cultivation of cells is essentially unfeasible as cells develop a synthetic 2D phenotype characterized by an altered gene and metabolic expression and, therefore soon after, lose their differentiated functionality. Thus, cells need to be grown in a 3D environment, where the cells are stimulated to maintain their native functionality. This requires the development of novel scaffold materials with sophisticated and adjustable properties, mimicking those of native tissues. It also requires new technologies to fabricate such 3D scaffolds with detailed control of the microarchitecture (8-9).

The most common technologies available today for the production of 3D scaffolds are according to Bakhshinejad, D'Souza, 2015:

• SLA (Stereolithography): A computer controlled laser beam is used to solidify liquid polymers and the objects are built up layer by layer

• SLS (Selective Laser Sintering): A computer controlled laser beam is used to melt a powder materials and fuses the powder into solid objects which are built up layer by layer

• LOM (Laminated Object Manufacturing): A computer controlled laser beam is used to cut out shapes layer by layer and the layers are glued together to form a three dimensional structure

• FDM (Fused Deposition Modelling): Polymer is extruded from a heated nozzle and guided to the desired position via computer control. Each layer is then fused together before the polymer solidifies

• 3DP (3 dimensional printing): A binder is printed out through a nozzle onto a powder bed to glue the desired amount of powder.

Most of these scaffold fabrication techniques require post-processing operations such as final curing at high temperature, removal of non-polymerized solvents, cutting of support structures etc. The majority of these methods are therefore not useful for the fabrication of 3D scaffold with simultaneous cell seeding as the cells would not survive such process. During almost 20 years of academic research tissue engineering research the scaffold based technologies never became clinically successful because the inability to achieve satisfactory cell migration into the 3D scaffolds. This is now, however, finally feasible with the use of 3D Bioprinting.

3.4 3D BIOPRINTING TECHNOLOGY

The drawbacks of pre-bioprinting tissue engineering technologies for scaffold production can be summarized as following according to Bakhshinejad, D'Souza, 2015:

- Poor reproducibility, Manual manipulation, not automated or robotic
- Laboratory scale, not industrial scale – lack of scalability
- 2D simple tissues, not 3D complex organs – not realistic tissue
- Lack of ordered tissue microstructure and lack of adequate strength

3D bioprinting uses a computer-controlled 3D printing device, 3D bioprinters, to accurately deposit cells and biomaterials into precise geometries with the goal being the creation of anatomically correct biological structures (8). 3D bioprinting belongs thus to family of Additive Manufacturing technologies, which are characterized as layer by layer additive production manner.

3.4.1 History

3D Bioprinting started as experiments carried out by Thomas Boland at Clemson University in 2000 when he placed bacteria suspension in an ink cartridge and then into an ordinary ink jet printer and successfully printed 2D patterns with living cells. He later replaced the bacteria suspension with mammalian cells and was able to successfully print with the human cells (Wilson, Boland, 2003). He filed the first patent in 2003 and patent was granted in 2006, see figure 3.

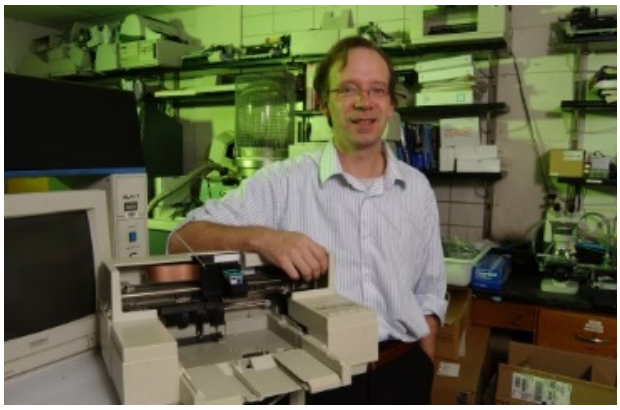


Figure 3 - Dr Thomas Boland at Clemson University with his inkjet printer

In 2004, Dr. Gabor Forgacs, professor at University of Missouri-Colombia, described the formation of cellular building blocks (bioink) and decided to developed the NovoGen bioprinting platform (Wilson, Boland, 2003). The first advanced bioprinters, NovoGen MMX Bioprinter, was constructed together with his team and Dr Forgacs founded the first bioprinting company in the world in 2007, his first printer see figure 4 and his lab see figure 5. Organovo went public quite early to raise the required capital for full commercialization. The company is a biotech company and it is now focusing on developing human tissue models that can be produced and delivered to customers while still being alive. Organovo Inc. started initially by selling their bioprinters, however, their bioprinter was very expensive and most labs in the world could not justify, during the early years, such large capital expenditure on such innovative technology. The revenues in 2016 are only 1,483M USD while the

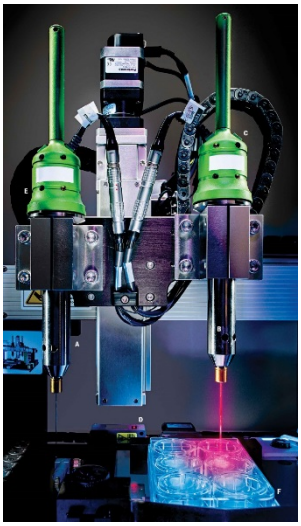


Figure 4 - NovoGen MMX Bioprinter developed by Dr G. Forgacs

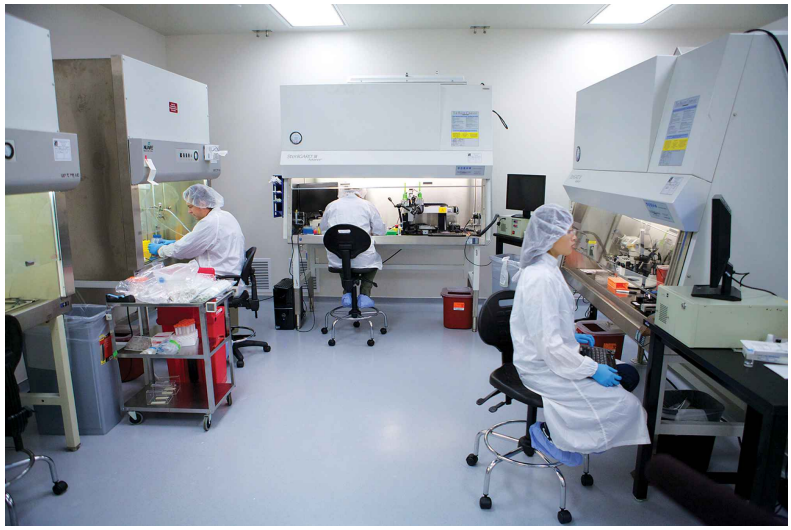
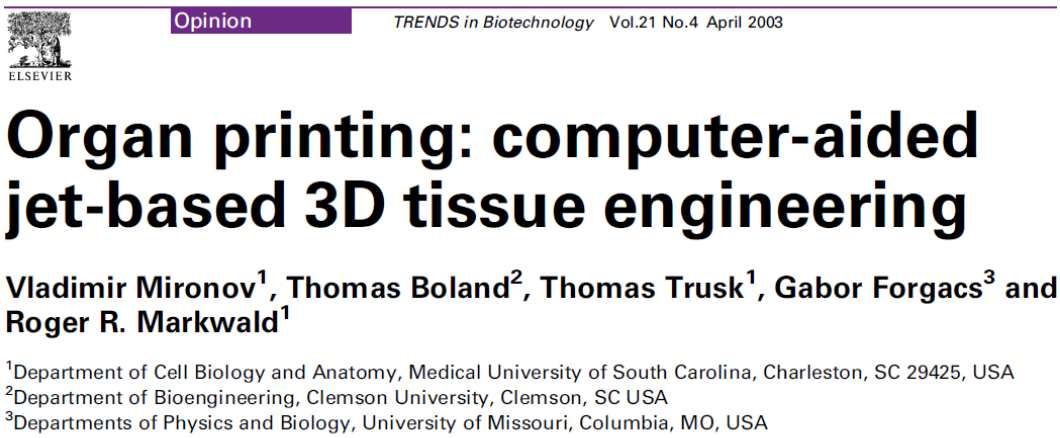


Figure 5 – Laboratory in Organovo in San Diego, CA, USA

company is spending 30M USD annually on R&D. The company was valued at 275M USD in December 2015.

During the same time Dr. Vladimir Mironov studied the bioassembly of tubular tissue constructs using bioprinting of self-assembled tissue spheroids illustrating sequential steps of layer-by-layer tissue spheroid deposition and the tissue fusion process. Interestingly, all three pioneers coauthored the first publication on organ manufacturing using bioprinting technologies in 2003 (Mironov, 2003), figure 6.



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ELSEVIER

Organ printing: computer-aided jet-based 3D tissue engineering

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Figure 6 - The first historical publication on organ printing (Mironov, 2003)

Since 2008, Wake Forest Institute for Regenerative Medicine at Winston Salem, NC, USA has developed applications for bioprinting of skin and built an in-house 3D bioprinter (Xu, et al., 2008).

The 3D bioprinting technology became better-known first in 2012 when several reviews on the subject were published in prestigious journals such as Nature Biotechnology (Murphy, Atala, 2014; Marga, et al., 2012; Derby, 2012; Atala, Yoo, 2015). Figure 7 summarizes the principles of the technology.

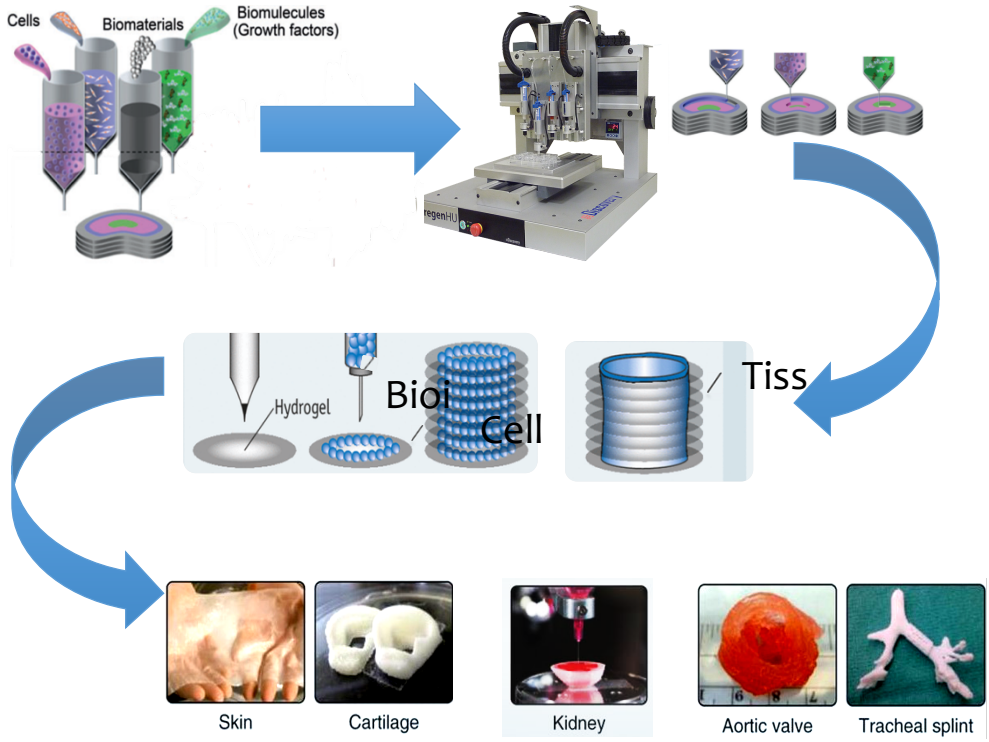


Figure 7 - Principles of 3D bioprinting technology adapted from Murpy, Atala, 2014

One of the corner stones of the technology is the use of cell suspension, a biomaterial in a liquid form, and additional components such as growth factors for cells to better survive and thrive. All of these components are typically loaded into separate cartridges. The cartridges are then fitted into so called print heads in the 3D bioprinter. The 3D bioprinter, such as one shown on the Figure 6, typically has 4 printing heads. The printing heads move in an XY stage controlled by a special language called G-Code. The G-Code language is generated using special software. In the beginning of the process, the 3D bioprinter operates as a traditional paper printer. It dispenses its ink on a n XY stage. After printing the first layer, the print heads move to the next layer (Z stage). The thickness of the layer is determined by material properties of the liquid biomaterial, but also by the movement of the Z axis (ibid.).

The following 3D bioprinting technologies are currently available according to Bakhshinejad, D'Souza, 2015:

- "Scaffold-free" printing

- Assembly of cell spheroids
- Laser Induced Forward Transfer (LIFT)
- Inkjet droplet printing
- Extrusion printing
- A syringe based extrusion printer
- Extrusion of cell-laden hydrogel

In the "scaffold free" printing, which is based on Dr. Forgacs´ patent and technology, which has been commercialized by Organovo, the cells are placed on the hydrogel support and then fuses into tissue like structures (Marga, et al., 2012). This technology typically uses agarose as a support hydrogel, which is extruded by one of the printing heads. Figure 8 shows the principle of the "scaffold free" printing. Different cell types can be placed onto an agarose bed and then after fusing has occurred, the agarose support can be removed. There are several disadvantages with this technology. Firstly, the resolution of the printed support structures is not particularly high because of the flow properties of the agarose solution before it hardens. Second, there are no advantages with the spatial resolution of 10 micron, which the robotic arm in the bioprinters offers when the cell suspension is deposited. Cells in the suspension will flow and stay in the predetermined position. In addition to that, the cell fusion process requires production of a extracellular matrix (biological material which is a part of the mammalian tissue). That process is very time consuming and typically requires weeks of growth. In summary, the "scaffold free" printing technology is not utilizing the full potential of what 3D bioprinting could offer.

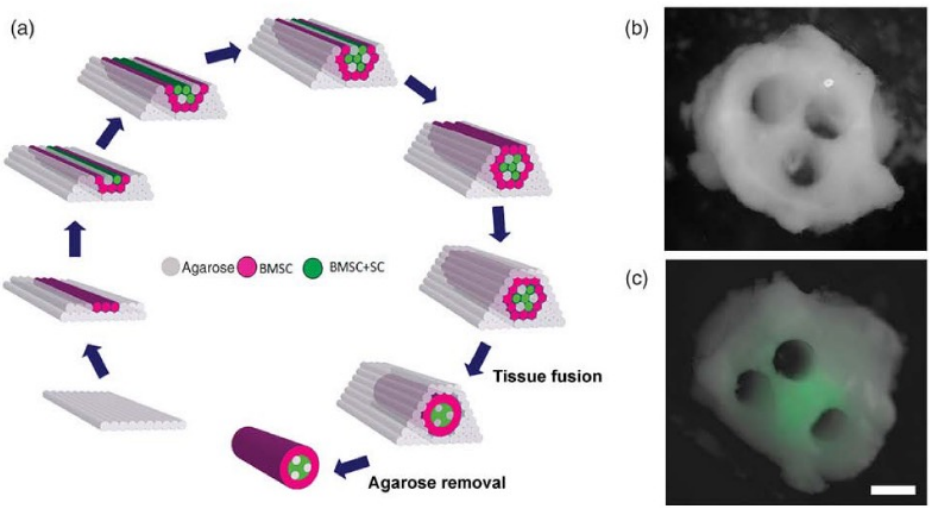


Figure 8 - Illustration of principle for "scaffold free technology" developed by Dr Forgacs and commercialized by Organovo (Marga, et al., 2012)

The technology developed by Dr. Mironov is somewhat related to the biological events occurring in actual tissue formation, which is the formation of cell spheroids and then an assembly of these spheroids into 3D tissue-like structure (Mironov, et al., 2009). The principle of this technology is illustrated in Figure 9. Dr. Mironov spent several years in the U.S. developing his technology and has now returned to Russia where he is heading the Regenerative Medicine Institute.

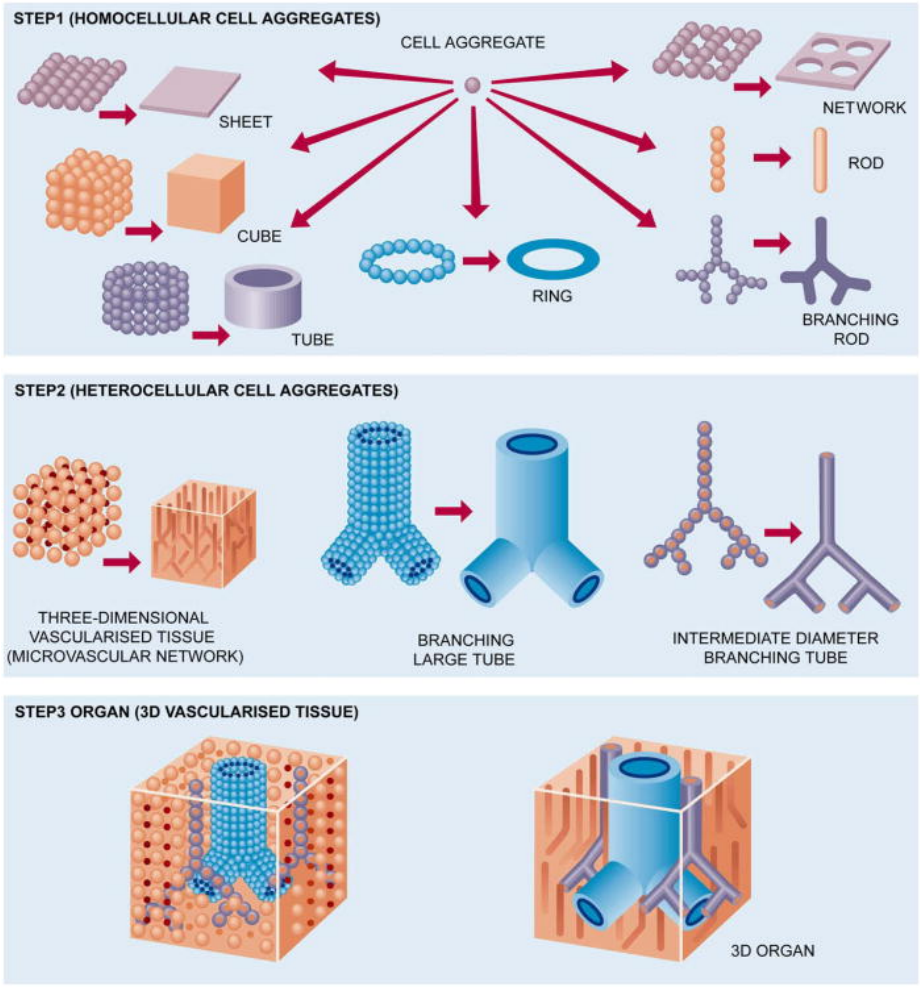


Figure 9 - Principles of assembly of spheroids 3D Bioprinting technology (Mironov, et al., 2009)

Another 3D Bioprinting technology is the Laser Induced Forward Transfer (LIFT), figure 10, technology developed in France by Dr. Guillemot and his coworkers. This technology is based on the use of lasers to create a cell-biomaterial particle that is energized from the laser and is then shot down with predetermined trajectory onto a plate. The LIFT technology has already been tested for repair tissues in animal studies (Catros, et al., 2011; Guillotin, Guillemot, 2011). It is, however, rather complicated since it requires meticulous preparation of the plate, coated with cells and biomaterial in a very precise manner. Therefore is this technology not suitable for beginners and early adopters.

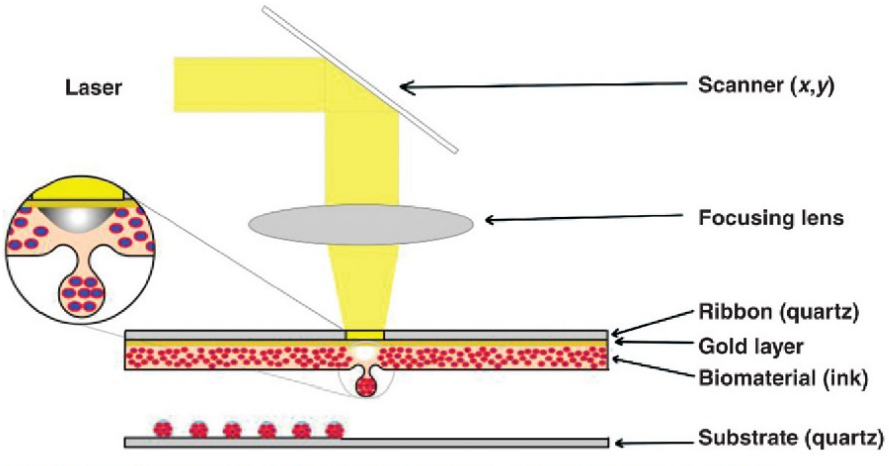


Figure 10 - Laser-assisted bioprinting principle (Catros, et al., 2011)

Inkjet droplet bioprinting and extrusion based bioprinting are relatively recently developed technologies and are very simple to use. Both require a 3D bioprinter with syringe fitted heads and a XYZ stage. In similarity to previously described 3D bioprinting technologies, the precision of the cell deposition is limited by the low viscosity of the cell suspension (Cui, et al., 2012). So when the cell suspension is dispensed from the syringe, it flows freely and the cells do not stay in place. This can, however, be changed if the cells are mixed into a liquid biomaterial or hydrogel prior to bioprinting. This process allows for a simultaneous printing of a scaffold biomaterial together with the human cells in suspension. For this to be feasible, several requirements must be met by the liquid biomaterial, such as cell compatibility (cells survival in the material) and rheological properties (behavior of a liquid under flow, also called "printability") (Blaeser, et al., 2013; Maher, et al., 2009; Visser, et al., 2015). Figure 11a shows the printing process for the inkjet bioprinters. Small volumes of liquids are dispensed by heating or by a opening and closing of piezoelectric valves into small droplets.

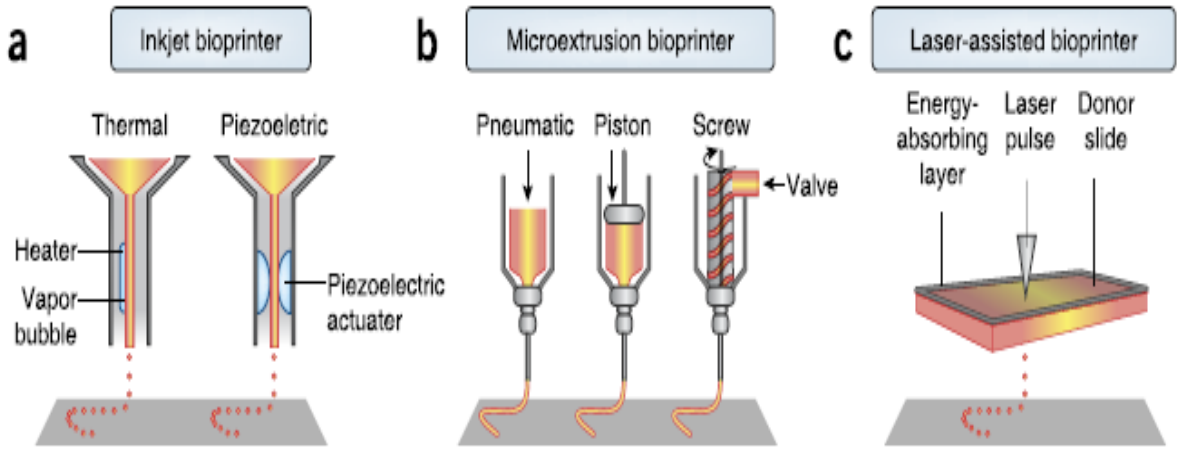


Figure 11 - Schematic illustration of 3D bioprinting using inkjet, extrusion and laser assistance (Murphy, Atala, 2014)

Figure 11b shows the microextrusion process, which can utilize either a pneumatic dispensing system where compressed air or another gas pushes the liquid through the syringe, or a mechanical system, which uses a piston to mechanically push the liquid out through the syringe or screw based extrusion system. Typical inkjet and and extrusion based 3D bioprinters can also be used for laser assisting deposition (see Figure 11c). Two big players in this 3D Bioprinting technology segment are; the German 3D Printing company EnvisionTEC with their 3D Bioplotter (Figure 12) and the Swiss company regenHU with their 3D Discovery (Figure 13) and Biofactory. Both are based on high precision XYZ stages and can be equipped with several different heads at the same time, controlling a wide range of parameters.

Figure 12 -3D-Bioplotter from Envisiontec

Figure 13 - Discovery from regenHU

Both brands are very expensive with the most cost effective model selling at 70,000 USD. The printing heads alone are in the range of 10,000 USD, giving a perspective on how capital intensive such purchase is. EnvisionTEC is a large 3D Printing Company selling 3D Printers for plastic and metals along with the printable filaments and materials. RegenHU is relatively young company situated in the rural region of Switzerland where many watch companies are operating. The heart of the RegenHu printer is a high precision XYZ stage, which is coming from an ABB robotic platform, which was donated to the University of Bern in nineties. It was then picked up and used as the robot to assemble watches (ibid.).

Another advanced and capital-intensive 3D Bioprinter on the market is BioAssemblyBot from Advanced Solutions, USA, with a six axis robotic arm and extrusion based heads (Figure 14). This bioprinter retails for 160,000 USD. In contrast, BioBot1 from the startup company BioBot established by 2 young electrical engineers from Pennsylvania sells for 10,000 USD and is based on a very simple syringe based extrusion system controlled by a pneumatic dispenser (Figure 15). Biobots has a competing equipment platform, however, lacks, a sustainable business model with bioinks and underlying expertise.

Figure 14 BioAssemblyBot from Advanced Systems -

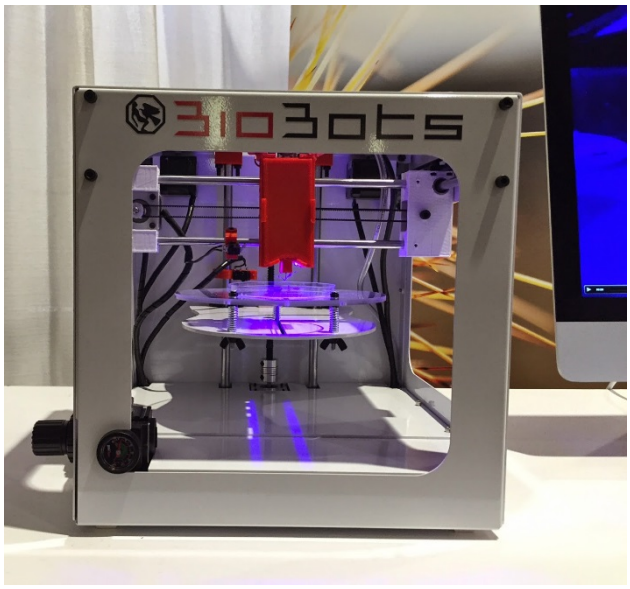


Figure 15- BioBot from BioBot

Table 1 summarized the history of 3D bioprinting by presenting available technologies for printing today.

Table 1 - summarizes current 3D Bioprinting technologies (Atala, Yoo, 2015)

Technology	Description
Inkjet	A pressurized reservoir of print material and either thermal or piezoelectric focus generate a pressure wave through the material, resulting in a small amount "jetting" out of the reservoir onto a surface.
Positive Displacement/Extrusion Bioprinting	Cellular bioink or hybrid biomaterial: cellular bioink is extruded through a size-controlled orifice for printing.
Laser	Laser focuses on a transfer slide, ribbon or drum containing the print material. The focused laser releases a plug of print material onto a receiving substrate.

3.4.2 Bioinks

The 3D bioprinting process requires a 3D bioprinter, cells, and a supportive biomaterial, which is called a bioink. Bioink is critical in terms of printability, cell viability, and support for the forming tissue. A bioink must show ideal rheological properties, which allows for printing of target structure. A "ketchup" like material is ideal, which means that it should have very high viscosity (almost solid-like) when in is solidified and it should have low viscosity when it is under shear stress (in the head of the printer being dispensed) (Malda, et al., 2013). Such fluids are called shear-thinning. The shear-thinning fluid should also transform into a solid structure quite fast after it has been printed. Hydrogel (gels that consist largely of water) materials are very attractive as bioinks because they provide s good combination of printability, which means the resolution of the printed structures, with optimal conditions for the cells (Weng, et al., 2007). When using hydrogels, it is possible mix the material together with human cells to prepare a cell laden construct. This method is what can be referred to as the CELLINK Method. The structure of a so-called cell-laden bioink must be designed in such manner that nutrients and oxygen can be transported to the cells that are encapsulated inside the hydrogel so that the cells can survive. Therefore, is it most common to print a structure called a "grid", in which one or a few layers of lines are printed on top of each other to resemble a waffle. Such grid is beneficial as it provides the ideal environment for the cells and is also stable from a mechanical perspective. Then once the scaffold has been

printed it has to be crosslinked to keep its integrity and to demonstrate mechanical stiffness. RegenHU has created BIOINK^{TM}, a hydrogel promoting cell growth for different cells by providing cell adhesion sites and mimicking the natural extracellular matrix. The first generation of the bioinks consisted of prepolymerized hydrogel precursors based on gelatine or collagen, which are UV or laser cured after extrusion from the bioprinter. There are, however, several disadvantages of UV crosslinkable bioinks based on collagen or gelatin. They have short storage time; have to be transported in dark containers and in -20 degree Celsius, which is very expensive for the end user. In addition to that, extended exposure to UV, as needed by the UV curing system, might damage the cells. Natural biopolymers such as alginate and hyaluronic acid have therefore recently been introduced to deal with the challenges of synthetic polymers and UV crosslinkable bioinks. Although, these materials generally have good biocompatibility and serve well as cell support, they have limited ability to be converted to mechanically tunable and robust scaffolds (ibid.).

3.5 THE 3D BIOPRINTING PROCESS FOR BIOFABRICATION OF HUMAN TISSUE AND ORGANS

3D bioprinting technology is being developed to fabricate living tissues and organs. In order to be able to do this, the human cells have to be used in addition to 3D bioprinter and bioinks. A 3D bioprinter can be described as an automated manipulator, which dispenses cells or cell aggregates with or without biomaterials (bioink). The bioprinter itself is simply a tool that reads a code of commands and performs such commands. The process of biofabrication of human tissue requires knowledge of tissue architecture and cell biology. Each tissue has a different microarchitecture and composition. Each cell type has different function in the human body and thus different properties. As an example, the heart has a function to pump the blood. The major component of hearth are cardiomyocytes, the specialized beating cells, that together, form the heart tissue and by beating together can perform the heart´s blood pumping function. To then biofabricate a heart requires understanding of biology of cardiomyocytes, growing of cardiomyocytes and then designing the CAD file (so called: blue print), which will control the motion of 3D bioprinter to produce a layer-by-layer cardiac tissue. It is important to understand that in contrast to 3D printing where 3D macro shape is of outermost importance, since the final product is produced by 3D printer, in 3D bioprinting the microarchitecture of the tissue is crucial. Another example of tissue which can be biofabricated is: skin tissue. Skin is the human body´s largest organ and is composed of two main layers, dermis (which is built of fibroblasts), and a top layer called: epidermis (which

consists of keratinocytes). Skin represents soft tissue and in the dermis layer, the fibroblast cells are only tissue producers, meaning they produce tissue as their main purpose. They proliferate and produce extracellular matrix ("meat of the skin"), which consists of Collagen I nanofibrils, elastin, proteoglycans and about 60% water. Once the skin layer is produced by the cells, the cells have no further function rather than maintain repair and renewal. Cartilage, another soft tissue that can be found in the human nose, ear, meniscus and knee joints is biofabricated by chondrocytes in the early organogenesis process and since these tissues are avascular (have no blood vessels) they have no capability for regeneration. Once these tissues are damaged, they cannot be repaired by body. The forth organ, which might be of interest to replace, is liver. The liver´s main function is to metabolize nutrients and break down toxins and this is done by highly specialized cells called hepatocytes. Each cell acts individually as a bioreactor taking in nutrients, breaking them down by enzymatic machinery, and releasing waste products. These cells are sitting on huge vascular branches. Biofabrication of the liver cannot be possible without biofabrication of complex vascular branches and simultaneously decorating such branches with hepatocytes (Atala, Yoo, 2015; Wilson, et al., 2016).

More details in the process of organ fabrication are described in appendix "Roadmap to Manufacturing Human Organs – basics".

The biofabrication process of tissue and organs can be divided into three stages, pre-bioprinting, 3D bioprinting and Post bioprinting (see Figure 16).

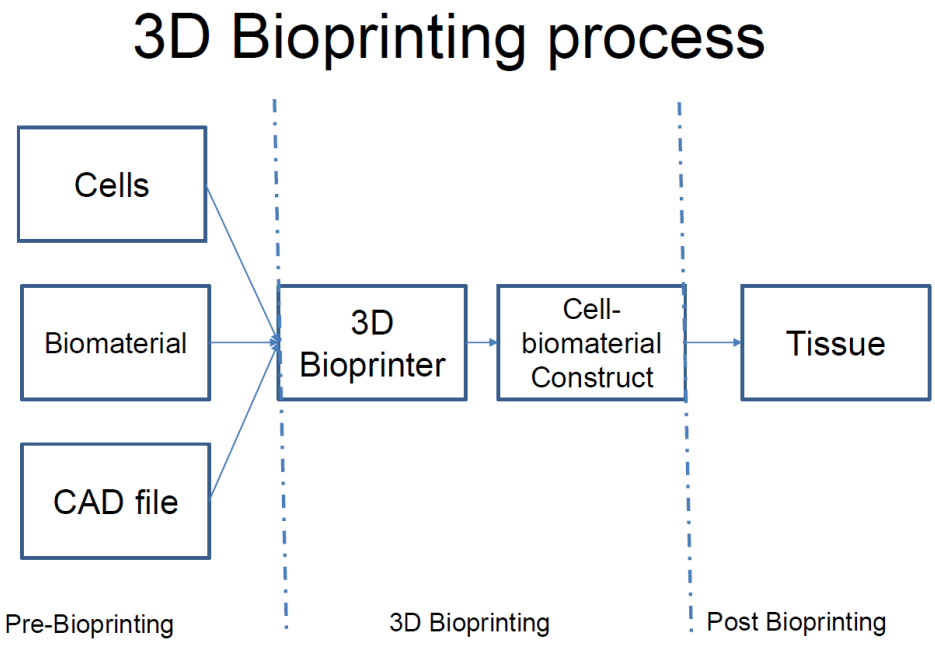


Figure 16 - Layout of 3D Bioprinting process (Wilson, et al., 2003)

The pre-bioprinting process requires selection and growing of cells, preparation of a suitable biomaterial (bioink), and a CAD file (blueprint) which will be used for controlling the 3D Bioprinter. Considering CELLINK already had developed a bioink and the bioprinter, there were two components missing for finalization of a complete package for bioprinting of human organs. In order to be able to offer the whole start-up package for customers who would like to enter the field of 3D bioprinting tissue and organs, there was the need to provide the human cells and CAD files. Both items were not readily available and the CELLINK team decided to provide them through strategical alliances and partnerships. The networking at the exhibitions and conferences combined with social networking made it possible. As described above, each tissue and organ requires different cells but the all the specialized cells are derived from stem cells in the organogenesis process (process of organ development) (ibid.).

Mesenchymal stem cells can be derived from the bone marrow, which is taken directly from donors' bone or from donors' adipose tissue (fat tissue). These cells can be isolated and expanded (proliferated) to almost unlimited amounts without losing phenotype (sustain its original type). Then they can be differentiated into cells producing bone, cartilage, muscle, ligaments, skin and fat (Farrell, et al., 2014; Scotti, et al., 2013). The access to mesenchymal stem cells is strategically important for the 3D Bioprinting community

4 CASE COMPANY – CELLINK

An introduction to the case company is presented in this section followed by the bioink and the bioprinter. CELLINK AB, officially founded at the end of January 2016, became after 6 months an important marketing player in the emerging 3D Bioprinting Industry and listed as number 7 in the world.

The Top 10 Bioprinters on the market according to the 3D Printing Industry (2016) are:

- EnvisionTEC's 3D Bioplotter Manufacturer Series + Developer Series

Technology: syringe-based extrusion

Materials: hydrogels, silicone, hydroxyapatite, titanium, chitosan

Price: up to $200,000+

- Organovo's NovoGen MMX

Technology: syringe based extrusion

Materials: cellular hydrogels

Price: not for sale

- RegenHU's 3DDiscovery + Biofactory

Technology: syringe based extrusion

Materials: bioink, osteoink

Price: up to $200,000+

- 3D Bioprinting Solutions' FABION

Technology: multiple (photocuring, electromagnetic and extrusion)

Materials: hydrogel, organoids

Price: not for sale

- BioBots BioBot1

Technology: syringe-based extrusion, blue light technology

Materials: agarose, collagen, alginate, polyethylene glycol

Price: $10,000

- **CELLINK Inkredible (new entry)**

Technology: syringe-based extrusion

Materials: CELLINK+ (improved CELLINK for chondrogenic differentiation), CELLINK A (alginate-based bioink) and other materials

Price: €5,000/9,000

- Ourobotics Revolution (new entry)

Technology: syringe-based extrusion

Materials: Collagen, Gelatin, Alginates, Chitosan and more.

Price: €12,500

- Advanced Solutions' BioAssemblyBot

Technology: six-axes syringe based extrusion

Materials: ND

Price: $159,999

- GeSim's Bioscaffolder 2.1

Technology: syringe based extrusion and piezoelectric nanoliter pipetting

Materials: polymers, high viscosity paste materials, alginate, calcium phosphate, silicon, cells and protein solutions

Price: $180,000

4.1 NANOCELLULOSE AS A BASE FOR A NOVEL BIOINK. CELLINK®

With the disadvantages of gelatine and collagen bioinks came a need for biomaterials with unique rheological properties combined with good printing fidelity and good cell compatibility. Nanocellulose, a biosynthesized in plants or produced by bacteria, can be supplied as a colloidal dispersion of nanofibrils in water (Klemm, et al., 2011). The size of the nanofibrils is similar to the size the collagen nanofibrils, which are found in native human tissue. This allows CELLINK to mimic the native tissue and to provide the human cells with an environment where they can thrive. Nanocellulose dispersion has very unique shear thinning properties, meaning that its viscosity becomes lower at a high shear rate. One of the major advantages of nanocellulose is that it can be oriented and assembled into 3D shapes with desired and exact mechanical properties (Feldmann, 2013). However, nanocellulose itself is not enough as a bioink material as it lacks the crosslinkability, meaning that it cannot

become rigid after printing. This challenge was overcome with the introduction of alginate into the nanocellulose mixture. Combining these two biopolymers at higher content of nanocellulose (80%) and lower content of alginate (20%) gives the bioink excellent printability and ability to crosslink with a binding agent after bioprinting (30). This became the base of the new bioink – CELLINK® (PCT Interational Application, 2015). Figure 17 shows how complex structures can be bioprinted with CELLINK®.

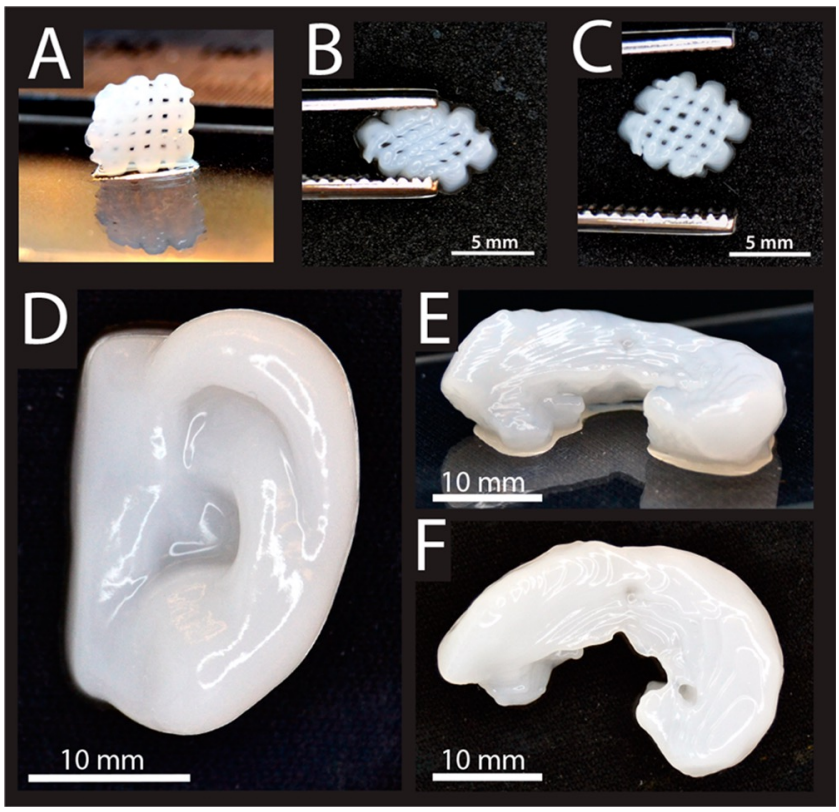


Figure 17- 3D printed grid (7.2 × 7.2 mm2) with CELLINK® after cross-linking. (B) The shape of the grid deforms while squeezing, and (C) it is restored after squeezing. (D) 3D printed human ear and (E and F) sheep meniscus. Side view (E) and top view (F) of meniscus (Markstedt, et al., 2015).

Another important factor of the bioink is the mechanical properties after crosslinking. The bioink should allow for movement of the scaffold without it breaking the structure. It should also resemble the native tissue as much as possible as this is an environment that the human cells are familiar with. The mechanical properties of the crosslinked CELLINK® are similar to the properties of human cartilage tissues such one that can be found in the human ear, nose or meniscus. The compatibility of CELLINK® with different human cell types have been evaluated and it has been determined through studies that the bioink provides excellent cell viability. In collaboration with Ulm University Hospital, the first larger in vitro study has been carried out using CELLINK® and human nasal chondrocytes (human cells that build

cartilage tissue). The results were very positive, showing production of human cartilage in CELLINK®. The CELLINK team presented the results for a scientific audience at the SELECT BIO 3D Bioprinting conference in Boston February 8-10, 2015. The audience was very impressed, showing great support and even commercial viability. The successful scientific presentation resulted in the invitation to the next SELECTBIO conference on 3D Bioprinting in Boston July 10-12, 2015. In the meantime, the packaging had been developed and a web shop was launched to evaluate the commercial need of the universal bioink. The introductory price was set at 99 USD per 3ml of CELLINK®. The sales were, however, limited even though orders were placed on day one of the launch. The team realized that there is a lack of cost effective 3D Bioprinters on the market and that providing bioink solely is not a sustainable business model in an industry where the printers cost 100,000 USD. In May 2015 the team decided to start to developing their own low cost bench top 3D bioprinter. The goal was set to introduce the bioprinter at the World Congress for Tissue Engineering and Regenerative Medicine in Boston, September 8-11, 2015. This allowed for only 4 months of product development. The CELLINK® bioink was scheduled to be officially launched already at SELECTBIO meeting in Boston in July in conjunction with completion of stability studies and packaging seletion. In addition to the portfolio of bioinks and bioprinters, the team determined that they will also provide all the consumables and related products needed for bioprinting. A device called the CELLMIXER was therefore developed and added to the CELLINK® package as the first in the world starting kit for 3D bioprinting (Figure 18) (CEILLINK, 2016).

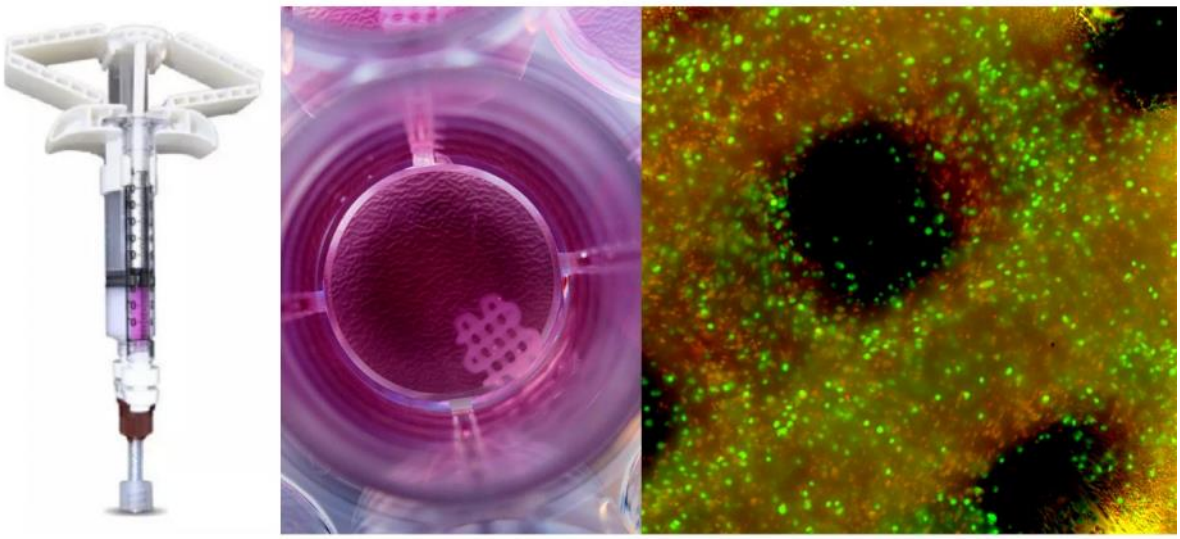


Figure 18 - The CELLMIXER was developed to get an accurate mixture of bioink and cells. To the right, a confocal microscope picture of the fluorescent cells (green and red spots) in the 3D bioprinted constructs showing a high distribution of cells (CELLINK, 2016)

Figure 19 shows the CELLINK® as it was launched in Boston in July 2015.

Figure 19 - The commercialized bioink product CELLINK® (CELLINK, 2016)

4.2 DESIGN AND PRODUCTION OF THE INKREDIBLE 3D BIOPRINTER

Once the decision was made to produce a low cost but high quality bioprinter, the work was initiated immediately. The access to other bioprinting platforms at nearby institutions allowed the team to view and better understand the limitation of other bioprinters marketed. A high focus on cell viability, ease of use, and cost effectiveness was established. The major components were produced locally in Sweden, as a matter of fact several parts were and remain 3D printed due to the high cost of mass production. One of features that the team invented during the design process was the ability to perform true bench top bioprinting. The team decided to offer two printers, one basic version named INKREDIBLE^{TM} and a larger version INKREDIBLE+^{TM} with a patent pending Clean Chamber Technology (Ref patent application coming soon), see figure 20.

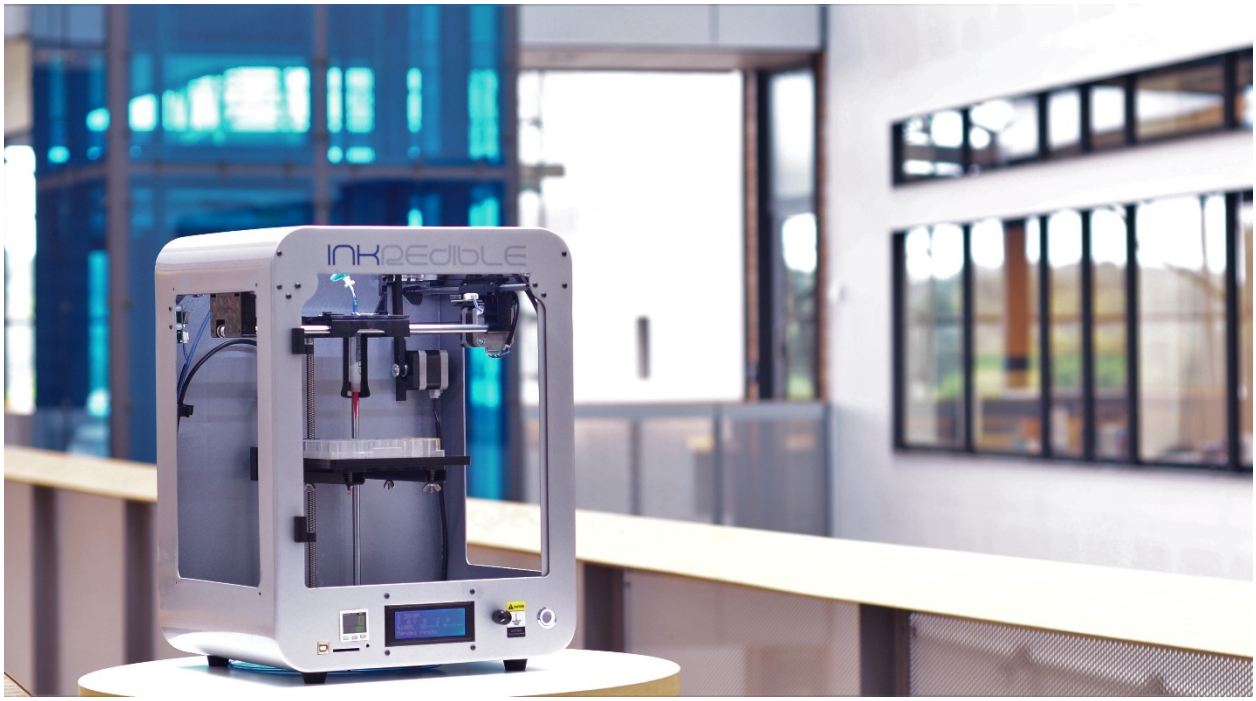


Figure 20 - The first bioprinter made by CELLINK

Figure 21 shows the CELLINK booth at the World Congress TERMIS in Boston September 8-12, 2015. The prototypes of both models were ready on time and operating according to the specifications. CELLINK´s booth at TERMIS was one of the most visited among all the exhibitors as no one expected another entrant into the bioprinters system field. The first customers showed great interest in ordering 3D bioprinter but also discussing collaborative projects. The first orders were signed later that fall (ibid.).

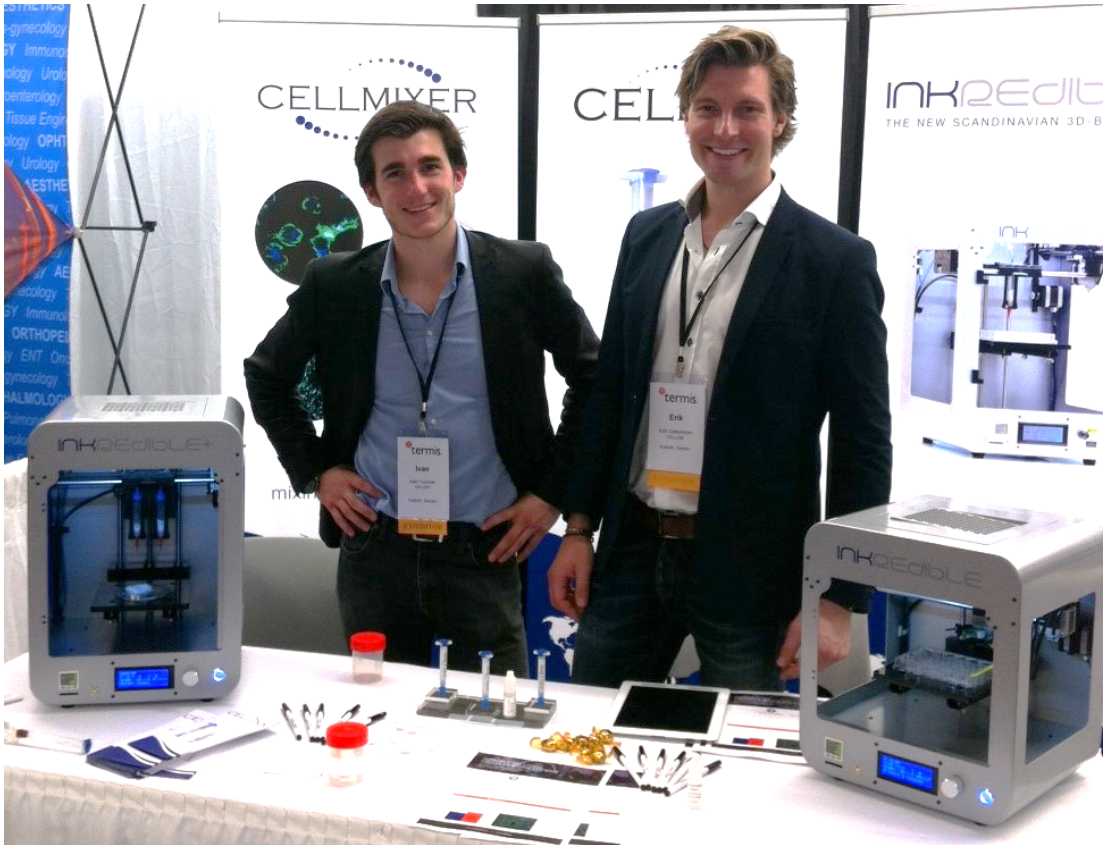


Figure 21 - Market introduction of CELLINK's 3D bioprinters. INKREDIBLE and INKREDIBLE+ and CELLMIXER at Word Congress for Tissue Engineering and Regenerative Medicine (TERMIS) in Boston, USA, September 8-11, 2015

4.3 STRATEGIC ALLIANCE WITH ROOSTERBIO

During the Boston SelectBIO conference in July 2015, the CELLINK team met with Dr. John Rowley, Founder and CEO of RoosterBio, an emerging stem cell company from Maryland, USA, and decided together to form a strategic alliance and perform R&D with bone derived stem cells and the nanocellulose based bioink, printing with the INKREDIBLE Bioprinter prototype. RoosterBio provided the cells and the CELLINK team did all the work with extremely short time to ensure release of the data for the TERMIS conference in Boston in September. The experiment included printing with a more advanced printer with an inkjet system, extrusion printing, and the use of the CELLMIXER. This extremely intensive R&D effort validate the previously developed protocols to print with stem cells with very high cell viability and also a validation that inkjet printing was causing cell death due to the nature of the printing process. This was something that was mentioned by several scientists but never shown in a comparative study. This resulted in a partnership between RoosterBio and CELLINK. This partnership paved the way for the introduction of a new product offered by RoosterBio and was released in September 2015, which was Ready to Print Cells (RTP cells).

Introducing living cellular bioink systems is a milestone in bringing 3D bioprinting to the market (Figure 22 and Figure 23).

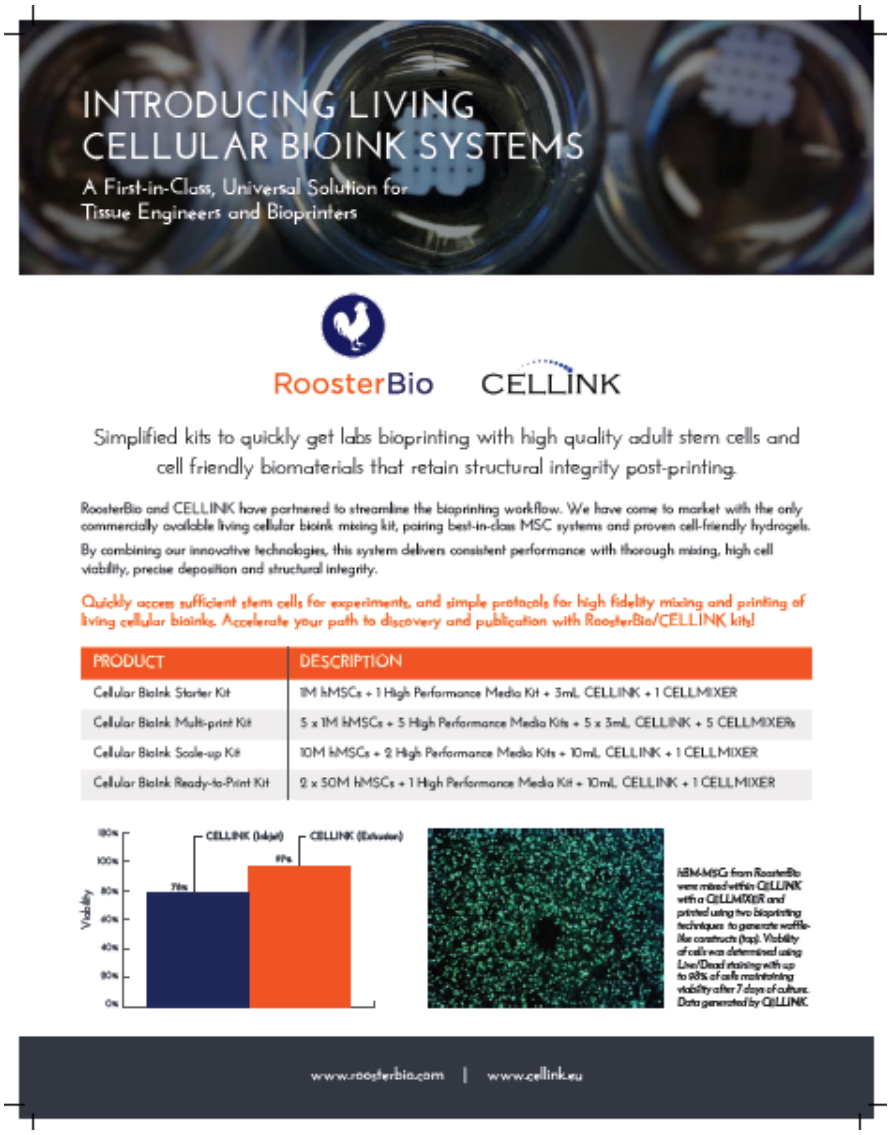


Figure 22 - Launch of Cellular Bioink Ready to Print

4.4 CELLINK & ROOSTERBIO LAUNSCH 1ST COMMERCIAL LIVING CELLULAR INKS FOR BIOPRINTING

Figure 23 - Launch of Cellular Bioink Ready to Print

Market´s reaction on introduction of living cellular bioink kits on the newspage 3D Printing Industry (2016) was:

"As we had anticipated, CELLINK, the Swedish startup that has made headlines lately with its bioprinting consumable cartridges and the INKREDIBLE low-cost bioprinter, is partnering with RoosterBio, a producer of stem cells. Now, the terms of that partnership have become clearer, as the two companies will collaborate on producing and commercializing the industry's first living cellular bioink kits."

4.5 BIOVERSE : BIOVERSE IS THE FIRST ONLINE PLATFORM FOR SHARING OF 3D MODELS FOR 3D BIOPRINTING

During the fall 2015, the team was extremely busy with the manufacturing of the 3D bioprinter to ensure full functionality prior to shipments, delivery of CELLINK cartridges, STARTINK kits, CELLMIXERs and marketing of the 3D bioprinters. The team had strategically decided to expand its product offerings with the last missing piece of the

portfolio, namely an online community for bioprinting. The time was too short for creating another partnership with a software company that could assist in this venture so the team decided to go the unconventional way by creating an end user community, namely: Bioverse, the first online platform for sharing of 3D models for 3D bioprinting (read below in Figure 24).

Figure 24 – Bioverse (3D Printing Industry (2015)

It was the missing step in the world of bioprinting. CELLINK did it! A new platform for CAD models for the printing of live cells. The Bioverse platform will offer bioprinting experts and beginners around the world with CAD models and protocols/procedures on how to print the structures with different cells.

"The goal with Bioverse is to provide the world with a self-sustainable community that allows users to upload and download models, discuss new and exciting bioprinting areas, and expand the global 3d bioprinting awareness," Gatenholm (CELLINK's Director of Operations) concludes. "We also see the emerging need of surgeons and doctors wanting to print tissue models and organs so that they can evaluate defects and challenges for surgeries. Bioverse will also offer a section for regular 3D printing so that medical practitioners can utilize these models for the purpose of practicing surgical procedures."

5 ANALYSIS

In CELLINK's case, the company is creating a new market segment – bioinks for 3D bioprinting of tissue model but at the same time it is introducing an innovation into the most demanding and established markets, which is testing platforms for cosmetics, skin care products, and personal care products. Since the market has not matured yet, and there is no mass segment, CELLINK as a company has a unique opportunity to become a large player and possibly establishing an industry standard.

5.1 WHAT HAVE WE LEARNED FROM THE CASE OF CELLINK AB

Through the case study of CELLINK AB we have learned that entering the new market in a technology focused arena requires extremely good contact with the buyers, which is happening today through social media, attending conferences and exhibition, and high flexibility to add new products that customers need. CELLINK has had a very short development process for each product, which can only happen through rapid product development, access to skilled key personnel, aggressive marketing and strategic alliances and partnership. The time window for entering the market in knowledge intensive industries is extremely short, in the range of few months, to make an impact. CELLINK AB made an entrance to the 3D bioprinting market by offering the first universal bioink in the world, however, the success came through the introduction of the complete package consisting of 3D bioprinters, consumables, bioinks and application knowledge, which included a partnership with an adult stem cell company and the launching of the BioVerse community. In addition, the education and training of the customers became an essential part of the business and provided market advantages. CELLINK AB is an excellent case study in which KIE model can be applied which is described in Table 2. The output of the development was the new firm formation (CELLINK AB was founded in late January 2016), exponential growth, and now entering a new phase of patent filing and knowledge creation in a more focused area. The development process in which human resources created growth formation of network and internationalization.

Table 2- Key aspects of KIE in CELLINK AB case according to the conceptual KIE model (How entrepreneurs do what they do, Edited McKelvey, Lassen, 2013

Accessing resources and ideas	
Opportunity recognition	• Hype of 3D bioprinting • Unmet needs for universal bioink • Space for low cost, high quality bench top 3D bioprinter • Needs for cellular bioink
Characteristics and traits of founders	• Hard working and result oriented
Founding team composition	• Young, educated and driven entrepreneurs
Knowledge bases	• Combination of business, knowledge, biomedical sector and engineering
	•
Human resources	• Access to students through collaboration with Handels, Sahlgrenska and Chalmers • Lack of skilled work force in the initial phase
Financial resources	• Created income from sales in early stage • Perfect timing with angel and early stage Institutional investors • Ability to charge upfront for products
Social resources	• Perfect home at Biotech Center where science, technology and education meets
Institutional influences	• Sahlgrenska Science Park, GU ventures, and Gothenburg provided good environment to grow

5.2 MANAGING AND DEVELOPING THE KNOWLEDE INTENSIVE ENTREPENURAL VENTURE

This part describes emerging growth of CELLINK AB between the founding of the company in late January by Erik Gatenholm and July 2016 when company became the hottest start-up of year in Sweden with several prestigious awards and amonst other meeting with the king, see figure 25.

Figure 25 – The Royal Majesty King of Sweden printing a nose

CELLINK AB financed all operations and processes through sales of the bioprinters and bioinks. The capital was sufficient to last at least a year, however, a strong desire to increase the speed to market and expansion resulted in the closing of a smaller seed round in April, 2016. With the seed funding, the company has focused very agile marketing and building up the organization with the first priority to reinforce the production capacity and sales to be able to deliver all the orders within few weeks. The major challenge in the early days were that the two founders, Erik and Hector, had to spend their nights constructing bioprinters instead of focusing on sales and marketing. With the seed funding, two production technicians could be hired and take over the production work. Another important aspect has been the filing of new patents and considering licenses and knowledge creation. The company has to prepare for future expansions and need to identify the path where investment will generate most return. Investment also need to create a unique company that can became a world leader in 3D Bioprinting.

5.3 WHAT IS INNOVATIVE WITH CELLINK

The innovation in the CELLINK has been the introduction of the nanocellulose based bioink with the unique combination of printing fidelity and cell compatibility. With the novel bioink, CELLINK made it possible to biofabricate two selected models of 3D soft tissues; skin tissue and cartilage tissue with controlled microarchitecture and great results. The ability to rapidly create an entry package for the emerging market segment is also innovative. The most important aspect behind CELLINK's innovation is the short path to market for all products generated by the company. CELLINK has had an extremely aggressive marketing strategy.

5.4 MARKET POTENTIAL

Table 3 summarizes competitive landscape of products that are available today on the market and the current price range (3D Bioprinting Market 2013). Skin grafts and artificial skin tissues are cadaveric or animal derived, which has been decellularized, whereas ReCell is a spray prepared in a clinical setting, originating from the patient own skin (Hu, et al., 2015; Gilleard, et al., 2013) that can then be reapplied.

Table 3 - 3D Bioprinted Skin: Competitive Landscape (3D Bioprinting Market, 2014-2030, Research Report, Roots Analysis

Product	**Price (USD)**
Skin Grafting	4 000-9 000
Artifical Skin	30 000- 40 000
ReCell	1 000
Bioprinted Skin	>200 (cost of only the hydrogel)

Figure 26 and 27 show the predicted bioprinted skin market with an expected market size of 1,78 billion USD within 10 years. It is not fully clear yet, however, how the market can be capitalized on. Would it be sales of 3D Bioprinters and bioinks together with a license for the companies and hospitals that will use it or the sales and delivery of bioprinted skin.

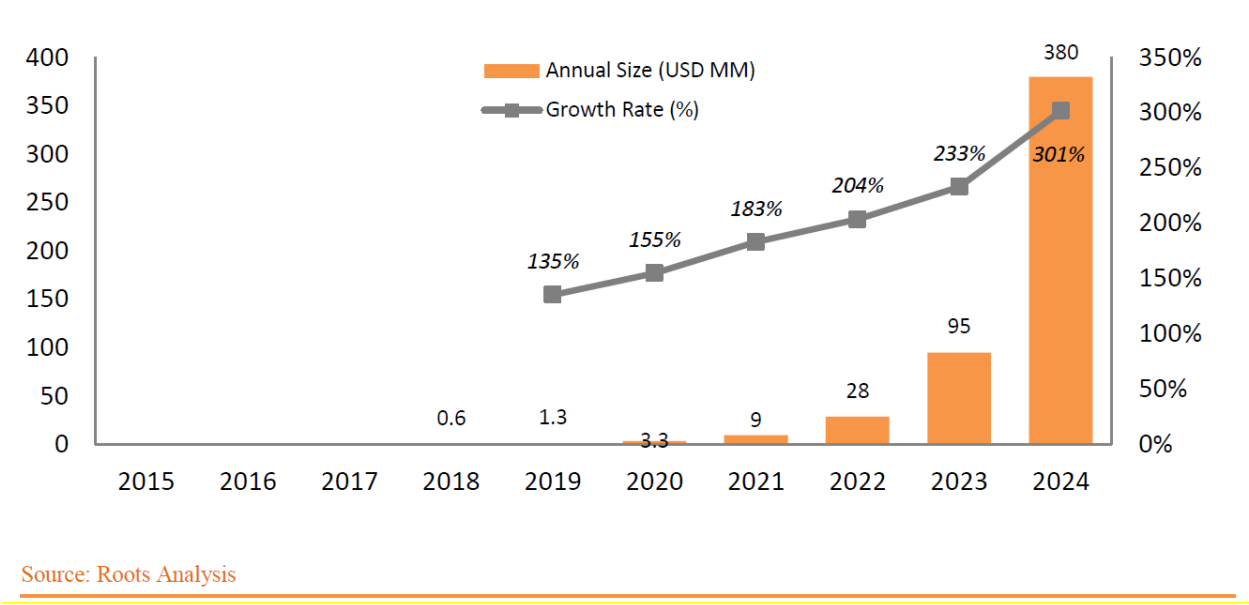
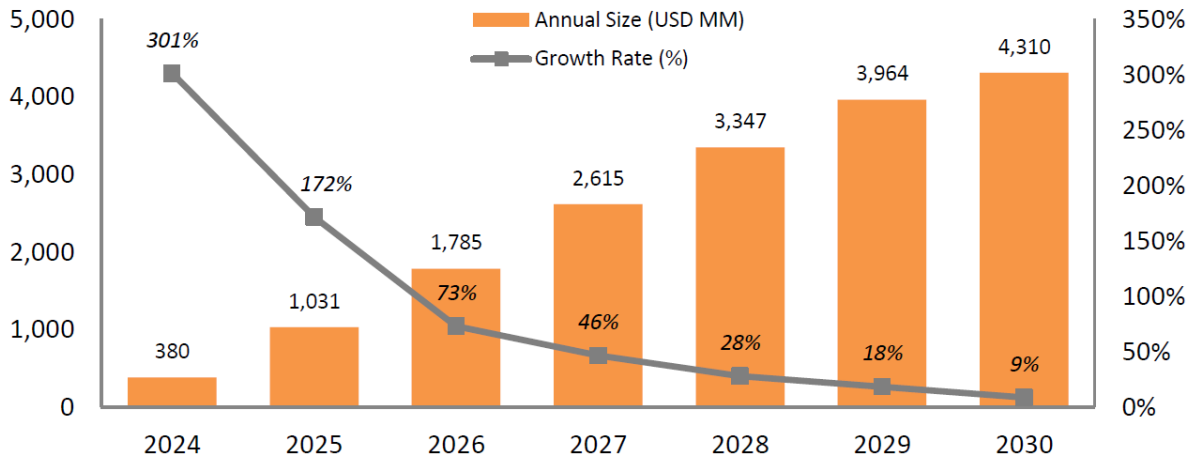


Figure 26 - 3D Bioprinted skin market, long term, base scenario (USD MM) (3D Bioprinting Market, 2014-2030, Research Report, Roots Analysis)



Source: Roots Analysis

Figure 27 -3D Bioprinted skin market, long term, base scenario (USD MM) (3D Bioprinting Market, 2014-2030, Research Report, Roots Analysis)

5.5 WHAT ARE THE SPECIFIC PROBLEMS OR DEMANDS

3D cell cultivation is gaining momentum not only in the academic research but also in industrial applications. While the translation from 2D to 3D cell culturing in the pharma industry is still in its infancy, the cosmetic industry is forced to employ in vitro organotypical tissue models for substance evaluation due to an animal test ban in 2013. Therefore, there is a huge demand for reliable standardized tissue models that are produced cost-effective in Switzerland and the rest of Europe.

For example, commercially available skin models are very expensive and rather simple in their composition (limited biological relevance). Furthermore, the need for customized skin models to address specific questions or disease models is increasing (concrete inquiry of Mibelle and DSM).

6 CONCLUSIONS

This thesis describes a novel model used for bringing a disruptive technology such as 3D bioprinting to the market. CELLINK AB, which is the first company in the world to commercialize a universal bioink for bioprinting, realized fast that the market for bioinks can only become substantial and sustainable when the market for related and complimentary goods grow. The development CELLINK's core bioprinting technology platform has been based on the scientific and technical expertise by the founders, Dr. Hector Martinez and Erik Gatenholm. The scientific knowledge has allowed the technology to be developed faster, more efficiently, and also with a focus on cost-effectiveness, which can be a challenge in early stages of new technology development. The development of CELLINK's business model and high focus on customer value has been a result of the founders' understanding of customer needs and the rapid market movements. The development of CELLINK's main organizational structure has been a result of the founders', mainly Erik Gatenholm, previous management experience but also new industrial management knowledge acquired through his education (Lassen & McKelvey 2013).

Providing bioprinters and bioink requires, however, also the services and education aspect so that the consumers can rapidly be educated. The strategic alliances with material suppliers and partnerships with cell suppliers have played an important role in paving the path to the market and success. The missing link, a library of CAD files of human tissues and organs, has been filled by creating the open source community "Bioverse". CELLINK AB found their niche by becoming the first 3D bioprinting company in the world that provides the entire introduction package for innovators to start with the 3D bioprinting technology. What made the commercialization process possible were mainly the agile marketing, rapid product development, and strategic alliances. But the future growth needs strategic decisions for expansion of sales, marketing, and manufacturing as well as the development of more application specific product offerings. The future market analysis provides a great outlook for 3D bioprinting of skin and cartilage. The case study CELLINK AB is analyzed using Knowledge Intensive Entrepreneurship, the KIE conceptual model.

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8 APPENDICES

Roadmap to Manufacturing Human Organs – basics