

Sample Patent Landscape Study

3D Bio-Printing of Tissues/Organs

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1. Introduction

1.1. 3D Bio-Printing

Bioprinting refers to an additive manufacturing technique that is used for the creation of organ/tissue-like structures that mimic the natural organs/tissues. 3D printers deposit layers of material otherwise known as bioinks to create various complex bodily structures including bones, skin, and even corneas. The technique is widely applicable to the fields of medicine and bioengineering.

Normally, the 3D bioprinting involves the same mechanism as that of the conventional 3D printers. In bioprinting, living cell suspensions are used for the printing. The required cells are normally extracted from a patient or, if this isn't possible, adult stem cells can be used and cultured into a bioink to 'print' an organ or tissues objects. These cells are normally held together through some sort of dissolvable gel or collagen scaffold that can support the cells and mould them into the correct shape.

3D bio-Printing involves more-or-less of the following steps:

- **3D Imaging:** Through a standard CT or MRI scan to get the exact dimensions of the tissue/organ.
- **3D Modeling:** Blueprint of the organ/tissue generated by means of AutoCAD software. Mainly aims to avoid the transfer of defects.
- **Bioink Preparation:** Bioink comprises of a combination of living cells, compatible base, like gelatin, collagen, etc. and cell growth/differentiation materials based on the requirements.

- **Printing:** Layer-by-layer deposition of the bioink based on the AutoCAD design.
- Solidification: Solidification or crosslinking may be aided by employing specific chemicals, UV light, or heat (also typically delivered via a UV light source).

Printing the living parts may prove to be a breakthrough technology in tissue/organ transplantation – harvesting the tissue-specific cells or stem cells from an organ/tissue recipient and printing them into a transplantable tissue/organ might aid to evade the complications linked with transplantations such as host rejection of the new organ and unending waiting period for an appropriate donor.

1.2. Market Potential

3D bioprinting market's growth is primarily steered by the ever-increasing use of 3D in cosmetology bioprinting the and pharmaceutical industries, technological developments in 3D bioprinters and biomaterials, and the increase in funds for research activities related to 3D bioprinting. The 3D bioprinting market is estimated to reach USD 1,647 million by 2024 from USD 651.6 million in 2019, at a CAGR of 20.4% from 2019 to 2024. Many factors have encouraged the industry players to increase and strengthen their existing production and supply capabilities, particularly in the emerging markets, which are predicted to experience growth at the highest rate.

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The Asia Pacific (APAC) market is anticipated to grow at the highest CAGR of 23.1% from 2020 to 2024. The growth is expected to be steered by the increase in the research activities, market demand for transplants, and the initiatives taken by market players for expanding their presence in the APAC and significant increase in the stem cell research.

India and China are projected to offer considerable growth opportunities for companies engaged in the 3D bioprinting research, owing to the growing demand for cosmetic surgeries, support from government bodies, and the less-stringent data requisites and regulations.

"Patent data shows 55% of total publication is pending applications. Higher percentages of applications point to a new or growing market"



2. Objective

- To perform detailed analysis of patenting activity pertaining to 3D bio-printing and to understand underlying technologies.
- To generate useful insights pertaining to 3D bioprinting technological field of study for the researchers at industry.
- Graphical representation of trends (Filing, Publication, etc.) from the mined data of relevant patents/applications.



3. Search Methodology



The first step is to create and define a patent set, which then serves as the basis of this study. Patent databases like Patseer have been used as our data sources. Search has been carried out in Abstract, Title and Claims fields of patent specifications by incorporation of Keywords and International Patent Classes.



4. Summary

Overview

This report analyses the global landscape of patents/applications filed in the technology area: 3D Bio-printing of Tissues/Organs

Patent Analysis

This report extensively analysed 700 patents/patent applications from the respective representative patent families, which resulted in the identification of 199 patents/patent applications relevant to the 3D Bio-printing of tissues/organs

- USA tops the innovator geography with 68 priority applications.
- APAC countries China and Korea are majorly innovating in the investigative technology.
- Magnetic and acoustic based 3D bio-printing would prove to be valuable technologies to be explored into.
- Ortho industry happens to be the major beneficiary of the investigative technology as evident from number of inventions related to bone tissues/cartilage.
- Gaining popularity of bio-printing of the delicate tissues like ocular tissues, Islets of langerhans, etc.
- With the increasing number of breast cancer patients worldwide, inventions related to the 3D bio-printing of breast tissues would prove to be beneficial. both in cancer research as well as regenerative medicine.
- Potential use of 3D printed cell culture systems that have potential uses in personalized medicine and the production of peptides/ antibodies/vaccines and other useful biological materials.



5. Technical Analysis

5.1. Bucketing of Relevant Patent Documents - Overall Technology

A set of 199 patent families were analyzed in depth to identify the focus areas of the patents related to 3D Bio-Printing technology.





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5.1.1. Dissection of Patents/Applications Pertaining To '3D Printer Type'



- Amongst the investigated 3D bioprinter types, extrusion bioprinting is the most used and discussed technology, followed by inkjet bioprinting mainly because of the ease of use that includes the employment of slightly viscous bioinks and creation of tissues with high cell density. Further, they are cheaper than most of the other 3D printing types.
- It is to be noted that the magnetic printing type failed to garner attention as evident from zero patent filings in magnetic bioprinting and would prove to be a valuable technology to be explored into.





5.1.2. Dissection of Patents/Applications Pertaining To '3D Printed Tissue/Organ'



- Bone tissue is the most sought-after tissue/organ for bioprinting followed by vascular tissues and cartilages. Ortho industry happens to be the major beneficiary of the investigative technology as evident from the number of inventions related to bone tissues/cartilage. It will be interesting to see the attention given to the bioprinting of delicate ocular tissues in future.
- 3D bioprinting of breast tissues is yet to gain importance. Currently, we see no inventions related to the same. With the increasing number of breast cancer patients worldwide, inventions related to 3D bioprinting of breast tissues will prove to be beneficial both in cancer research, regenerative and personalized medicine.





5.1.3. Dissection of Patents/Applications Pertaining To 'Cell Type Used for 3D Bio-Printing'



As expected, stem cells are the preferred cell type for 3D bioprinting for the purpose of generating various types of tissues/organs, because they offer several advantages over differentiated cells, including the potential for autologous tissue and differentiation into multiple cell lines.





5.1.4. Dissection of Patents/Applications Pertaining To 'Matrices Material'



Collagen proves to be the most sought-after material for hydrogels/matrices/ scaffold/support material, followed by gelatin and alginate, respectively. The data from the current analysis evidences the importance of ECM proteins for 3D bioprinting technology. Synthetic macromolecules and Matrigel have proven to be of great value as the preferred materials and are gaining importance in the recent times.





5.1.5. Dissection of Patents/Applications Pertaining To 'Utility/Applications'



Tissue regeneration is the main application of the 3D bio-printed tissues/organs followed by implants and transplants. Tissue models generated using 3D bioprinting have proven beneficial in drug discovery and cancer research.



5.2. Leading Assignee Analysis





- ORGANOVO INC (12 patents/applications) is the top applicant/assignee. Sizeable number of applications are from the leading assignees originating from the APAC region, preferably from China and South Korea.
- CELLINK CO LTD (9 patents/applications) is the second most leading innovator from Sweden but preferred filing its innovations in USA.



5.3. Leading Assignee across Technology

5.3.1. Dissection of Leading Assignees across '3D Printer Type'

	3D Bioprinter Type										
Leading Assignees	Generic 3D Printer	Extrusion Bioprinting	Inkjet Bioprinting	Laser-assisted Bioprinting	Others						
ORGANOVO INC		9	3		1						
CELLINK CO LTD		1									
BIOINKSOLUTION INC		4									
POSTECH ACADEMY INDUSTRY FOUNDATION											
SHENZHEN INST ADV TECH											
REVOTEK CO LTD		2	1	1							
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD	1	2									
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY			1								
UNIV SUN YAT SEN											
UNIV OREGON HEALTH SCIENCE		2									
UNIV OF JINAN	1	1									
TR BIOFAB CO LTD	1	1									
QINGDAO UNIQUE PRODUCTS DEVELOP CO LTD		2									
PRELLIS BIOLOGICS INC		3	3	3							
INVENTIA LIFE SCIENCE PL	1										
CELLHEAL AS		1									



Leading assignees prefer the employment of extrusion type bioprinters for printing of tissues/organs, with maximum inventions recorded by ORGANOVO INC (9 patent/patent applications), followed by BIOINK SOLUTION INC (4 patent/patent applications).



5.3.2. Dissection of Leading A	Assignees	across 'Cel	l Type'
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	3D Bioprinting Material												
			-	Cell	Гуре								
Leading Assignees	Muscle / Smooth Stem Cells Muscle Cells		Fibroblast	Endothelial Cells	Epithelial cells	Tumor / Cancer Cells	Bone Cells	Others					
ORGANOVO INC		4	6	3	3		1	6					
CELLINK CO LTD	1	3	2	1	1	1	1	6					
BIOINKSOLUTION INC	4	5	3	4	4		4	5					
POSTECH ACADEMY INDUSTRY FOUNDATION		1	1	1									
SHENZHEN INST ADV TECH				1				4					
REVOTEK CO LTD	3	3	1	3	2	1	1	2					
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD		1	1			2		2					
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY	1	1	1	1	1		1	2					
UNIV SUN YAT SEN								1					
UNIV OREGON HEALTH SCIENCE			1	2		1	1	2					
UNIV OF JINAN		1	1	1				1					
TR BIOFAB CO LTD		1						1					
QINGDAO UNIQUE PRODUCTS DEVELOP CO LTD		2					2	3					
PRELLIS BIOLOGICS INC	1	1	1	3	1			3					
INVENTIA LIFE SCIENCE PL	1	1	1	1	1		1	1					
CELLHEAL AS		2						2					



- Stem cells are the ideal cell types to generate the preferred tissues/organs using 3D bioprinters. Endothelial cells and Fibroblasts follow the suite. ORGANOVO INC is the only company to prefer more innovations using fibroblast cells (6 patent/patent applications).
- Tumor/Cancer research through bioprinted tumor tissues is hardly researched by the leading assignees, with a maximum of only 2 patent/patent applications from MEDPRIN REGENERATIVE MEDICAL TECH CO LTD.



			-	-	-		30	Bioprinting Mate	rial			-	-	-	
							Hydrogels /	Matrices / Scaffo	ld / Support						
Leading Assignees	Generic Hydrogel	Synthetic Macromolecules	Collagen	Gelatin	Alginate	Decellularized Biological Material	Hyaluronic Acid	Chitosan	Cellulose	Matrigel	Fibrin	Silk Fibre / Fibroin	Fibrinogen	Agarose	Others
ORGANOVO INC	3		3	1		2	1				1		1		4
CELLINK CO LTD	1		1	1	2	1	1	1	6		2	1			2
BIOINKSOLUTION INC			3	5									2		
POSTECH ACADEMY INDUSTRY FOUNDATION						4						1			
SHENZHEN INST ADV TECH	2		2	3	2		1	2		2				2	1
REVOTEK CO LTD		2	2	2	2		2	2			2			2	2
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD	1			2	1		2								2
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY	2		1		1	2									
UNIV SUN YAT SEN		2				1									
UNIV OREGON HEALTH SCIENCE	2														
UNIV OF JINAN		1		1											
TR BIOFAB CO LTD			1	1	1	1				1	1			1	
QINGDAO UNIQUE PRODUCTS Develop co LTD		2	2	2	2		1	2							
PRELLIS BIOLOGICS INC		1	2	2	1		2								1
INVENTIA LIFE SCIENCE PL		2	2	2			1	1	2		2				
CELLHEAL AS	1		2	1	1		1	1	2		1	1			2

5.3.3. Dissection of Leading Assignees across 'Matrices Materials'



- Though collagen is the main support/hydrogel material preferred overall, Gelatin (23 patent/patent applications) is the preferred material by the leading assignees with maximum exploration by BIOINK SOLUTION INC (5 patent/patent applications).
- Companies from the APAC region (e.g. REVOTEK CO LTD, INVENTIA LIFE SCIENCE PL) have significantly explored the use of synthetic macromolecules for the bioink composition in comparison to the companies from the well-developed regions like USA (PRELLIS BIOLOGICS INC).
- Interestingly, CELLINK CO LTD majorly preferred cellulose (6 patent/patent applications) for the 3D bioprinting bioinks, which is also the maximum used material recorded by any of the assignees.



5.3.4. Dissection of Leading Assignees across '3D Printed Tissue/Organs'

							3D Pr	rinted Tissue / Or	gan					
Leading Assignees	Generic Tissue / Organ	Renal	Blood Vessels / Vascular / Lumen Tissues	Skin	Bone	Liver	Lungs	Cardiac / Cardiovascular	Breast Tissue	Adipose Tissue	Cartilage	Ocular Tissue	Tumor Tissue	Others
ORGANOVO INC	1	5	3	2	2	2	1			2			1	4
CELLINK CO LTD	1	2	2	3	3	2	2	2			1			1
BIOINKSOLUTION INC	2		1		1						1			3
POSTECH ACADEMY INDUSTRY FOUNDATION	3													1
SHENZHEN INST ADV TECH										2				3
REVOTEK CO LTD	1		2		2						2			
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD	1												1	1
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY	2				1									
UNIV SUN YAT SEN	3													
UNIV OREGON HEALTH SCIENCE													2	1
UNIV OF JINAN	1		1											
TR BIOFAB CO LTD	1		1	1				1						
QINGDAO UNIQUE PRODUCTS DEVELOP CO LTD	1				1						1			1
PRELLIS BIOLOGICS INC		2	1	1	1	1	2	1						2
INVENTIA LIFE SCIENCE PL	1													
CELLHEAL AS										1				2



- Bone, blood vessels/vascular/lumen tissues and renal tissues are the chiefly produced tissues/organs by the leading assignees.
- Interestingly, none of the identified leading assignees have inventions related to ocular tissues and breast tissues which are predicted to have a huge share in regenerative medicine markets in the days to come.



5.3.5. Dissection of Leading Assignees across 'Utility/Applications'

	Utility / Applications													
		Regenerative Medicine / Tissue Defects			Tissue Mim	ics / Models								
Leading Assignees	Reg M Tiss			Drug Discovery	Toxicity Cancer Evaluation Research		Others	Implants	Cell / Tissue Culture System	Transplantati on	Others			
ORGANOVO INC		5		6	6	6	4	1						
CELLINK CO LTD		5		1	2	1	4	3		1				
BIOINKSOLUTION INC		3	_		2		2	1		1				
POSTECH ACADEMY INDUSTRY FOUNDATION		1		1						1				
SHENZHEN INST ADV TECH		4		1			3							
REVOTEK CO LTD		4		2			2	1						
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD						2	1							
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY		2		1	1	2					1			
UNIV SUN YAT SEN		3												
UNIV OREGON HEALTH SCIENCE				1		2	1							
UNIV OF JINAN		2									1			
TR BIOFAB CO LTD		1					1							
QINGDAO UNIQUE PRODUCTS DEVELOP CO LTD		2						1						
PRELLIS BIOLOGICS INC		1					2	2						
INVENTIA LIFE SCIENCE PL							1		1					
CELLHEAL AS		1						1		1				



- Regenerative medicines, drug research and cancer research are the main areas of interest for the leading assignees. On the other hand, the implant systems have gained considerable attention from the leading assignees as well.
- INVENTIA LIFE SCIENCE PL is the only leading assignee that explores the use of 3D printed cell culture systems having potential uses in personalized medicine and the production of peptides/antibodies/vaccines and other useful biological materials.



6. Non-Technical Analysis

6.1. Trend Analysis – Earliest Invention in 3D Bio-Printing Across Geographies



- Overall priority filing data infer that the 3D bioprinting technology had garnered attention as early as 2009 in USA and Canada. However, there had been considerably less focus on this technology until 2013 with scattered inventions being applied here and then.
- The investigative technology gained considerable popularity after 2013, with the maximum filings being recorded during the year 2018 (23% of the filings).
- USA used to be a forerunner, however, in the current scenario the APAC countries like China and Korea have been regularly innovating in the investigative technology.
- China and Korea are the only geographies to register inventions during the year 2019.
- In furtherance, China has registered the maximum inventions (9% of the filings) during the year 2019 and is the highest registered by any geography.



6.2. Trend Analysis – Legal Status Analysis





- 55% of active applications indicate the advancement in investigative technology and the possibilities of pathbreaking inventions in the days to come.
- ➢ It is also to be noted that the inactive patents (20%, that includes rejected/refused/suspended and withdrawn/surrendered patents) are way less than that of the active patents/ applications (80%), signifying the major researches happening in the investigative technology.



6.3. Assignee Based Trend Analysis

6.3.1. Assignee Category





➤ 46% of the patents/patent applications are filed by the academics and the research institutions. The contribution by these organizations to the investigative technology is substantial. In addition, they are competing with the companies actively involved in this research.



6.3.2. Leading Assignees across Earliest Priority Years





The priority filing trend of the leading assignees indicate a gradual growth of the technology from 2013. The trend reflects the peek during 2016. It is evident that North America generated the maximum amount of revenue in the year 2015-2016 in the global 3D bioprinting market. This might be attributed to the enormous availability of the printable materials i.e. cell-laden bioinks, as well as the printing & assembly methods, starting from 2013.



6.3.3. Leading Assignees across Earliest Priority Countries

Leading Assignee	Earliest Priority Country						
	AU	CN	KR	SE	NS		
ORGANOVO INC (US)	2				10		
CELLINK CO LTD (SE)				4	5		
BIOINKSOLUTION INC (KR)			6				
SHENZHEN INST ADV TECH (CN)		5					
POSTECH ACADEMY INDUSTRY FOUNDATION (KR)			5				
MEDPRIN REGENERATIVE MEDICAL TECH CO LTD (CN)		4					
UNIV SUN YAT SEN (CN)		3					
UNIV OREGON HEALTH SCIENCE (US)					3		
UNIV OF JINAN (CN)		3					
UNIST ULSAN NAT INST OF SCIENCE TECHNOLOGY (KR)			4				
TR BIOFAB CO LTD (KR)			3				
REVOTEK CO LTD (CN)		5					
QINGDAO UNIQUE PRODUCTS DEVELOP CO LTD (CN)		3					
PRELLIS BIOLOGICS INC (US)					3		
INVENTIA LIFE SCIENCE PL (AU)	3						
CELLHEAL AS (NO)					3		



Of all the leading assignees, ORGANOVO INC and CELLINK CO LTD are the only companies which opted to file their patent applications in Geographies other than their actual country of incorporation. ORGANOVO INC which has it headquarter in USA had filed patent applications in Australia, while CELLINK CO LTD has its headquarter in Sweden, but it has more filing in USA than its native country.



6.4. Patent Classification Based Trend

6.4.1. Major IPCs – Main Class



6.4.2. Major IPCs - Sub Class





6.4.3. Leading Assignees across IPC – Main Classifications





6.4.4. Leading Assignees across IPC - Sub Classifications





Key Patents

Patent/Publication No.	Field of Invention
<u>US20160213764A1</u> BATU BIOLOGICS INC	The patent application relates to 3D bioprinting of tumor cells for the production of cancer vaccines containing antigenic properties similar to in vivo growing tumors, which cannot be currently replicated under existing 2-dimensional tumor culture means of generating cell lines.
<u>WO2019109127A1</u> INVENTIA LIFE SCIENCE PL	The patent document relates to a bioprinter for fabricating three- dimensional (3D) cell constructs that can be used for drug discovery, personalized medicine and general cell biology.
EP3538643A1 ORGANOVO INC	The patent document relates to the use of 3D printed intestinal model for assessing the ability of a candidate therapeutic agent to reverse, reduce or prevent intestinal injury by a potential toxic agent using a three- dimensional, engineered, bioprinted, biological intestinal tissue model.
<u>CN106139249A</u> QINGDAO SANDI BIOTECHNOLOGY CO LTD	The patent document relates to a preparation method of a multipolymer artificial cornea that has excellent mechanical performance, and biocompatibility.
WO2020081890A1 NORTH CAROLINA STATE UNIV	The patent document relates to a method of ultrasound-assisted 3D bioprinting that utilizes piezo transducers to generate longitudinal bulk acoustic waves within the bioink fluid matrix.
KR101954953B1UNISTULSANNATINSTSCIENCETECHNOLOGY	The present invention discloses a bio-ink composition for three- dimensional printing, which has potential application in generating cell- based biosensors
WO2020089840A1RESTECHNIONRESDEVELOPMENT	The present invention discloses a miniature bone mounted robot configured to perform minimally invasive orthopedic surgery coupled with regenerative three-dimensional bio-printing technology.
KR20170075499APUSANNATUNIVINDUSTRYUNIV COOP	The present invention provides a configuration of a three-dimensional bio-printer system using a virus that allows control of various fluids.
<u>US20200024560A1</u> US NAVY	The present invention discloses a microfibrous scaffold, that can be made of a composite bioink, and that can have endothelial cells directly embedded within the scaffold using an additive manufacturing process that has potential applications in nanomedicine.



Appendix A - References & Credits

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- 11. https://www.nature.com/articles/nbt.2958
- 12. https://www.3dnatives.com/en/3d-bioprinters-main-manufacturers-081020194/#!
- 13. https://www.sciencedirect.com/science/article/pii/S0142961219306350
- 14. Title Image Credit: Shutterstock



Appendix B – Definitions Of IPC Classes

IPC Subclass	Definition
A61L	METHODS OR APPARATUS FOR STERILISING MATERIALS OR OBJECTS IN GENERAL; DISINFECTION, STERILISATION, OR DEODORISATION OF AIR; CHEMICAL ASPECTS OF BANDAGES, DRESSINGS, ABSORBENT PADS, OR SURGICAL ARTICLES; MATERIALS FOR BANDAGES, DRESSINGS, ABSORBENT PADS, OR SURGICAL ARTICLES
A61L 27/20	Polysaccharides
A61L 27/22	Polypeptides or derivatives thereof
A61L 27/36	containing ingredients of undetermined constitution or reaction products thereof
A61L 27/38	Animal cells
A61L 27/40	Composite materials, i.e. layered or containing one material dispersed in a matrix of the same or different material
A61L 27/52	Hydrogels or hydrocolloids
A61L 27/54	Biologically active materials, e.g. therapeutic substances
C12N	MICROORGANISMS OR ENZYMES; COMPOSITIONS THEREOF; PROPAGATING, PRESERVING, OR MAINTAINING MICROORGANISMS; MUTATION OR GENETIC ENGINEERING; CULTURE MEDIA
C12N5/07	Animal cells or tissues
C12N5/071	Vertebrate cells or tissues, e.g. human cells or tissues
C12N5/077	Mesenchymal cells, e.g. bone cells, cartilage cells, marrow stromal cells, fat cells or muscle cells
C12N5/0775	Mesenchymal stem cells; Adipose-tissue derived stem cells
B29C	SHAPING OR JOINING OF PLASTICS; SHAPING OF MATERIAL IN A PLASTIC STATE, NOT OTHERWISE PROVIDED FOR; AFTER-TREATMENT OF THE SHAPED PRODUCTS, e.g. REPAIRING
B29C 34/106	using only liquids or viscous materials, e.g. depositing a continuous bead of viscous material
B29C 34/20	Apparatus for additive manufacturing; Details thereof or accessories therefor
B29C 67/00	Shaping techniques not covered by groups B29C 39/00-B29C 65/00, B29C 70/00 or B29C 73/00



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