

3D printing applications for the treatment of cancer

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ARTICLE INFO

Keywords:

3D printing
Additive manufacturing (AM)
Applications
Cancer
Treatment
Tumour

ABSTRACT

Purpose: Additive manufacturing (AM) is an innovation in today's medical field. It helps create a patient-specific 3D model of bones, nerves, organs and blood vessel. Now, doctors and surgeons have successfully applied this technology to plan different types of treatments and also cancers. The purpose of this paper is to study the requirements and applications of AM for cancer treatment.

Methods: Today AM is used for the application of regenerative medicine. It can help develop and improve in-vitro models in the tumour microenvironment. Thus, to identify its applications, related research papers on AM for cancer are studied.

Results: 3D printing technology has a unique capability to manufacture tumour models. It helps to understand the status of the whole tumor. Here in this paper, we studied the capabilities of AM technologies for cancer treatment. This study discusses necessary process steps, followed by 3D printing and finally identified significant applications of these technologies for cancer treatment with a brief description.

Conclusion: 3D printed tumor helps to provide faithful studies on metastasis. These models create a promising platform to construct biomimetic models. By accurate manufacturing of in vitro model, this technology seems to be the best tool to facilitate complex treatment, surgery and therapies. It shows great potential for the printing of organs. This technology is time-saving and avoids time-consuming processes. It has been analysed that AM helps in reducing the duration of treatment of a cancer patient. Researchers are focusing on reducing pain during therapies. They have also tested 3D printed tumor models for different drugs, to eliminate the risks. These models play a significant role in courses of treatments.

1. Introduction

Globally cancer is being reported as the cause for a large number of human deaths and treatment-related trauma. Additive Manufacturing technologies provide excellent capabilities which offer a better solution for a cancerous tumor. Model printed by this technology help to understand the disease behaviour of a patient. We can construct a 3D object using layer by layer technique. The quality of the object by manipulating the machine parameters and input materials are increased. Additive manufacturing is a useful tool to manufacture patient-specific implants which can further be used successfully for surgical planning.¹ AM technologies consist of 3D imaging/scanning, 3D printing and software supports. These technologies can fulfil different challenges and provide several benefits in education, research and patient care.^{2,3} It achieves a higher level of flexibility by using different software and can increase the accuracy and reliability of the process.

This technology thus creates innovation in the medical field.

AM is used for the development of new tools and equipment in the medical field. This technology is useful for the fabrication of customised maxillo-facial prosthesis implants and another medical device. It provides good collaboration between doctors, radiologists, surgeons and engineers. This technology shortens research and development time of new products. It is a new method of personalised medicine, design and development of implants and medical devices.^{4,5}

3D printing plays a vital role to enhance the ability of design and development of the product in the medical field. It manufactures customised shape product to fulfil individual patients' requirement. Researchers and medical students can now study fracture/disease in detail without any risk. Its applications are for the planning of complex surgical procedures, training, simulation, diagnosis, and manufacturing of patient-specific implants.^{6–8}

3D printing is a useful technology to produces accurate prototypes

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<https://doi.org/10.1016/j.cegh.2020.03.022>

Received 15 December 2019; Received in revised form 8 March 2020; Accepted 19 March 2020

Available online 25 March 2020

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as well as finished parts. This technology can print implants, bio-compatible surgical guides with a wide variety of materials. The efficiency of existing products is improved by modification in the design of the product. 3D printing is useful for speeding up the first stages of product development in lesser time and cost. It allows researchers and students to study artefacts in detail without any risk.^{9–11}

There are vast applications of 3D printing in the engineering fields. It is readily applicable to make new engineering designs. This technology is used to create cast mould, sub-scale turbine blade mould and various other useful engineering components. Products printed by 3D printing technology are useful for modern engineer's training and help to create an innovative product as per the customer's requirement.^{12,13} This technology is now also applicable in the field of cardiology. This paper describe brief about the capabilities of 3D printing for the treatment of cancer.

2. Additive Manufacturing

Additive manufacturing technology sets provide new applications in the treatment of cancer. It consists of different scanning/imaging, 3D printing technologies along with designing, scanning and printing software. The data of the cancer patient is taken quickly by using Computed tomography (CT) and Magnetic Resonance Imaging (MRI) technologies, and further these images are converted into 3D digital computer-aided design (CAD) models by using different software's. This CAD model can be printed quickly by using appropriate 3D printing technology.^{14,15} Here a complex shape is printed (manufactured) layer by layer, and finally, makes a full 3D physical object, and this can be used for treating some types of cancer. 3D printed model of the tumour shows the exact location of this tumour in the patient's body.¹⁶

Additive manufacturing becomes an important tool for the design and manufacturing of custom parts which can be easily used during the replacement of patients' parts. Its applications are in many fields such as medical, engineering, aerospace, design and manufacturing of prototype before starting the full production.^{17,18} For modification in the design of the existing product, 3D scanners and Imaging machines are now available, which allows creating a digital 3D object from a physical object. 3D Scanner is non-contact scanning technology used to scanned object in the form of point cloud data without any physical contact.

Its applications are in designing of customised orthotic, prosthetic, tools and devices as per the requirement.¹⁹ It provides a modified concept to the industry as per the desired shape and dimension. 3D scanner increase design quality and efficiency of the final product. AM provides excellent potential for doctors and researchers to create new ideas to understand complex human systems.^{20,21}

3. What is cancer?

Cells are an essential part of our body which maintains a human body healthy in a controlled manner. Cancer cell starts out of control of the patient by which a tumor creates abnormal cells. Cancer forms a tumor and interferes with body function. It continuously grew and spread through the metastasis process.²² Cancer is a large group of disease which rapidly spreads to other organs and tissues. For example, it begins from the lungs and also spreads in the liver. This disease creates an abnormal growth of cells. It forms cells which are not required and cause the growth of a tumor. The primary treatment process of this disease is chemotherapy, surgery, radiation therapy, drug therapy and stem cell transplantation.²³ For the treatment of cancer, 3D printing offers new dimensions by quickly creating a physical 3D model which precisely shows the patient's tumor. The CAD model of the image can be analysed for better planning of cancer-related treatments and surgery. The significant benefit of this technology is to reduce the risk and improve the treatment outcome. A surgeon can now practice on the procedure to improve the skill using an exact patient-specific 3D model.

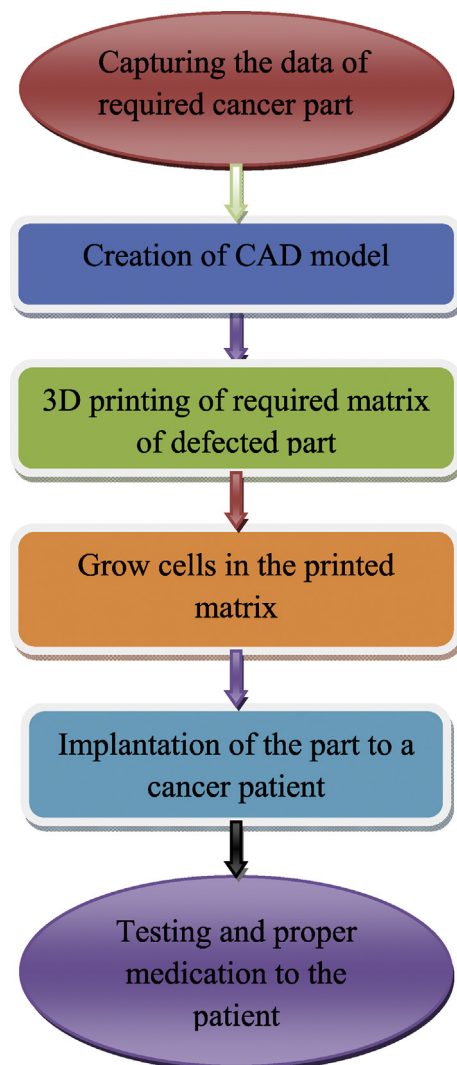


Fig. 1. Process of 3D printing for cancer treatment.

4. Research objectives

3D printing already explores its capability for the printing of tissue, organs and cells. Now a day, this technology also helps in the treatment of cancer. It makes safer surgery which can be performed accurately and precisely. The surgeons can easily create a 3D model of the cancerous part and then analyse them before surgery. This patient-specific model is the best approach during the treatment of invasive cancer surgeries. It helps to predict the recovery after performing the surgery. 3D printed model eliminates various risk factors during the surgery. This innovative technology can assist doctors with better planning and treatment. 3D printed patient-specific tumor model make a better treatment decision. This article addresses the following research objectives:

- RO1:** To understand the need for AM and capabilities of AM for cancer treatment;
- RO2:** to study the process of 3D printing for the treatment of cancer;
- RO3:** to identify significant applications of 3D printing for cancer treatment;
- RO4:** to study the future scope of this technology regarding the better treatment of cancer.

Table 1
Some basic applications of 3D printing for cancer treatment.

S No	Applications	Description	References
1	Accurate replica of the cancerous part	<ul style="list-style-type: none"> • Doctors can get precise treatment of cancerous body part of the patient by creating a personalised replica model • Help to analyse cancer cells in just a small fraction • Accurate 3D printed replica helpful to provide better dose to fight Cancer • 3D printed model is a better option to get precise information as compared to 2D scan report 	Perica and Sun, 2017 ³⁰ ; George et al., 2017 ³¹ ; Wu et al., 2018 ³²
2	Printing of cancerous tumours	<ul style="list-style-type: none"> • This technology prints cancerous tumours for undertaking research and development • 3D printed cancerous tumours provide better ideas as compared to available 2D/3D imaging • Having the ability to customise treatment beyond cancer therapies • Helps surgeon to prepare life-changing surgery • Successfully used to predict response for different treatment of the patient 	Stone, 2014 ³³ ; Baek et al., 2016 ³⁴ ; Kim et al., 2017 ³⁵
3	3D phantoms of tumours and organs	<ul style="list-style-type: none"> • CT/MRI scan data is used to create 3D phantoms of tumours and organs for better treatment of the patient • Helps to provide proper dose to kill cancer cells • Used for the treatment of tumours which spread in the bones • It enables doctors for personalising treatment and fast recovery of the patient • Provide idea for precisely mimic flow inside the tumor • It is time and cost-effective process to create detail and complex phantoms 	Kijima et al., 2014 ³⁶ ; Hodgdon et al., 2018 ³⁷ ; Haleem et al., 2020 ³⁸
4	Treatment of tumour tissue	<ul style="list-style-type: none"> • This technology is used for the treatment of tumour tissue and quickly identifying specific cancer types of disease • 3D printed patient-specific tumour provides a proper introduction from different angles • Perfect 3D printed replica provide accurate shape and size of the tumor and its surrounding area • Create innovative advancement in research and clinical cancer therapeutics 	Dupret-Bories et al., 2018 ³⁹ ; Lupulescu and Sun, 2019 ⁴⁰
5	Accurate geometry of tumour	<ul style="list-style-type: none"> • It quickly produces a 3D model of the tumour with precise geometry which helps for better treatment • It deposits living cells, layer by layer for the effective treatment of cancer • This technology used imaging technique for the proper analysis of tumour 	Chepelev et al., 2018 ⁴¹ ; Fan et al., 2019 ⁴²
6	Study cancer growth	<ul style="list-style-type: none"> • 3D printing model seems helpful to study the process of cancer growth • Printed models can be used for surgical planning • 3D printed organ, tissue and tumor provide precise information regarding the abnormalities 	Lindegard et al., 2016 ⁴³ ; Ballard et al., 2018 ⁴⁴
7	Better teaching tool	<ul style="list-style-type: none"> • Helpful to study tumor growth and spread of the cancer • AM technologies are useful in model making, and then these models can be gainfully used • Scanning inputs can also be analysed by software, and then simulation can also be done. • Provide knowledge about the symptoms of this disease caused by various reasons 	Libby and Silberstein, 2017 ⁴⁵ ; Garcia et al., 2018 ⁴⁶ ; Javaid and Haleem, 2019 ⁴⁷ ; Haleem and Javaid, 2019 ⁴⁸
8	Monitoring of cancer treatment	<ul style="list-style-type: none"> • Accurate ideas about where the tumour is located in the patient body • Help to monitor different stages by using support software when provided with scan data • It makes easier treatment by identifying the stages of diseases • Different biocompatible materials printed by this technology can increase patient care 	Westerman et al., 2016 ⁴⁹ ; Santiago et al. 2019 ²² ; Javaid et al., 2019 ⁵⁰ ; Kim et al., 2019 ¹⁶
9	Skin cancer treatment	<ul style="list-style-type: none"> • 3D printing address optimum planning of radiation and normal anatomy of the tumor • It enables radiation for the treatment of skin cancer and superficial tissue • This technology creates a reality of handheld models 	Priester et al., 2014 ⁵¹ ; Witowski et al., 2017 ⁵²

5. Need for Additive Manufacturing for cancer treatment

Treatment of cancer is quite challenging and is undertaken through different types of therapies. 3D printing is part of AM used for printing CAD file of the tumor. Tumour imaging is analysed through AM software can be used to analyse the mechanism of various physiological aspects in a patient. This technology prints tumor model for a better understanding of patient and doctors. By using this technology, there is a possibility to collect information regarding the cells of a tumour.²⁴ In the medical field, this technology can focus on reducing pain during cancer treatment. It can be thought of using long-lasting cancer treatments, like radiation therapy and chemotherapy. It is applied

successfully for breast cancer.^{25,26} In this process tumour, cells are taken and print tumour. Thus, further helps to different tryout drugs and sort out the best treatment for the patient.²⁷

6. Process of 3D printing for cancer treatment

3D printing manufactures a physical part, directly from a 3D CAD file, when provided in Standard Triangulate Language (STL) format. It creates a part layer by layer, which is opposed to subtractive manufacturing technologies. 3D printing is direct manufacturing of finished product without any requirement of tools and fixture. It plays a vital role in product development.^{28,29} This technology reduces the cost of

product development and cycle time. It is easy to use and create an ecofriendly cost-effective product. Fig. 1 shows the process of 3D printing for cancer treatment.

The first step is to capture the required data of the patient using different scanning and imaging technologies. This data is converted into a CAD 3D model using different software and further, convert it into the required printable format. After the conversion of data, this data is used in 3D printing technology for the printing of the required matrix of the defected part of a cancer patient. Finally, this part is implanted in the patient body, or it is also used for testing and to provide proper medication to the patient.

7. 3D printing applications for cancer treatment

AM software helps to simulate several medical procedures by producing and analysing the required specified CAD models, further, they can be printed. Tumor model manufactured by this technology provides accurate behaviour of the patient body. Doctors can surgeon can analyse the tumor and take its advantage for better treatment. Table 1 discusses the different applications of 3D printing for cancer treatment.

The applications of this technology are extensive, starting from imaging to software modelling. It can create a 3D model from image files, which can be helpful to show the detailed flow of radiopharmaceuticals in the patient's body. Thus, it helps for the treatment of other tumours like cancers of nerves cells in children, thyroid cancer and bone tumour. Effective communication is required in today's medical field.^{53–56} This technology is right to plan a reconstructive surgery by manufacturing accurate implant with different materials. This technology is now used for the printing of tissues, organs and stem cell printing. With the input of biocompatible material, a scaffold is efficiently manufactured by which cells and tissue can grow and creates their shape. It is a useful technique to build a 3D hollow vessel structure.

8. Discussion

Millions of deaths are reported due to the cause of cancer. 3D printing is an innovative technology used to construct the 3D model layer by layer, which is helpful for the treatment of cancer patient. This technology uses different types of materials as well as a natural material with living cells/tissue.^{57–59} It used a combination of biomaterials, bioactive additives or cells. 3D models are used for tumor biology, which includes 3D cell migration, cell proliferation, nutrient etc. It is an emerging method for the manufacturing of scaffold, which is helpful to grow living tissue. It has the capability to build a complex and heterogeneous structure which was not easily possible with traditional technique. This technology investigates cellular physiology in a controlled manner. Doctors can now print entire prosthetic limbs with an accurate patient match. Today 3D printing is used to print models of tissues with blood vessels, prosthetic parts, bones, cardiovascular models, heart valves, ear cartilage, and synthetic skin. These printed models provide proper information on cancer tumours.^{60–62} It showed the status of growing tumours for the individual treatment of the patient with the use of AM. This technology is used for the treatment of kidney cancer. It quickly develops tissue therapeutics, which is helpful for regenerative medicine and therapeutic discovery.

9. Future scope

In future, applications with AM technologies will provide towards the effective and precise treatment of cancer patient. This technology has great potential to fulfil the shortage of donor. It overcomes the challenge of whole organ replacement by creating a functional one. 3D printing accelerates the development of cancer immunotherapy. Doctors are accelerating the 3D printing impact to increase cancer patient care. In future, this technology can be applied to manufacture in

vitro models of metastasis. It produces effective results for tissue engineering. In upcoming days, it will become a perfect tool to create human arms, hands and legs which will work as a normal. With its reconstruction ability, it can save millions of lives. It will enable to print human skin which can be helpful for the treatment of skin cancer.

10. Conclusion

3D printed tumour models can easily convey inside information of a patient's body. It is used for developing personalised anti-cancer drugs. The main challenge of this technology is to create an effective treatment of cancer. Scientist and researcher analysed the development of tumour mesh by using an accurate model printed by this technology. 3D printed model also helps for the better diagnosis of cancer treatment. This technology has emerged for the treatment of liver-related surgeries. It is helpful to check the status/condition of liver disease. The 3D printed tumor has the ability to analyse the tumor and provide the proper drug for the patient. These proper drugs help to bind cancer cell for better treatment of the patient. It addresses cancer with the help of personalised treatment modality. 3D printed surgical guides are helpful for the cancer patient while undergoing chemotherapy. 3D printed medical tools and devices are helpful for precisely removing the tumor. It has excellent capability to create complex & customised 3D cell biology. In future, 3D printing will be applied to provide proper dose to kill cancer cell without damaging the healthy tissues.

Declaration of competing interest

None.

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