Chapter

Applications of Three-Dimensional Printing Technology in Radiotherapy

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Abstract

Nowadays, three-dimensional (3D) printing technology has been used for rapid prototyping of high quality printed objects. This technology has taken a special place in the field of medicine, and today this technology plays an important role, especially in the field of radiotherapy. Radiotherapy is a main option for treating and management of various types of cancers. Personalized radiotherapy requires precise details. For this reason, it is very important to carry out the exact treatment design at the clinical. 3D printing technology is considered a promising method that can be effective in the treatment of each person in a specific way and as a complementary and promising method to help in integrated treatment and special equipment for each patient. In this chapter, various applications of this technology in radiation therapy have been discussed. This narrative review summarizes the applications of 3D printing technology to develop patient-specific bolus, brachytherapy applicators, phantoms, filters, immobilization and grid therapy devices for more personalized radiation treatment.

Keywords: 3D printing technology, radiotherapy, cancer, bolus, brachytherapy applicators

1. Introduction

Surgery, radiotherapy and chemotherapy are common methods in cancer treatment [1]. Almost more than two thirds of patients with cancer, are treated via radiotherapy [2]. The main goal in radiotherapy is maximum dose delivery to the tumor while minimizing the side effects caused by the treatment. In the past decades, new radiotherapy technologies such as Intensity Modulated Radiation Therapy (IMRT), Image Guided Radiation Therapy (IGRT), Stereotactic Radiosurgery (SRS), Stereotactic Body Radiation Therapy (SBRT), and three dimensional treatment planning in Brachytherapy have been introduced. Such advances in radiotherapy have led to an increment in the absorbed dose in the tumor area and a decrement in the received dose by healthy tissues in the treatment area [3–5]. Therefore, it is very important to carefully implement the treatment design. Although the advent of new radiotherapy technologies has led to the reduction of errors relevant to the reconstruction of the patient's geometry, there are some errors in the accessory's productions. So, the use of medical devices is not suitable for each patient.

Nowadays, 3D printing technology is considered as a promising method that can be effective in the treatment of each person individually. Hence, there is a great interest in application of the 3D printing technology in the radiotherapy process. Today, this technology has attracted a lot of attention for making patient-specific accessories, dose modifiers, phantoms and several other devices in radiotherapy [6–9].

Recently, several studies have been conducted in the field of 3D printing technology in radiotherapy, in terms of making patient-specific boluses, brachytherapy applicators, fixing devices, etc. Therefore, in this chapter, the basic applications of 3D printing technology in radiotherapy have been summarized.

2. Three-dimensional printing

The concept of 3D printing was conceived in the 1970s, but the first experiments date back to 1981. One of the main applications of 3D printing technology is the manufacturing of medical equipment. The first use of 3D printing technology in medicine appeared shortly after its invention. In 1990, Palser et al., first transferred Computed Tomography images of the human skull and knee joint in the solid three-dimensional polymer model making system and printed the 3D models using the stereolithography technique [10]. The process of creating a physical object from a digital model is considered as a simple definition of 3D printing technology. In comparison with the common printers, 3D printers create a 3D physical model from the desired target. Creating an object with a 3D printer requires a 3D-digital model. A 3D-digital model can be created by scanning a set of 3D images or drawing it using CAD design software, as well as using data from Computed Tomography (CT) or Magnetic Resonance Imaging (MRI), obtained [11]. Then, this 3D digital model is sent to the printer in STereoLithography (STL) format. Finally, a 3D model is created layer by layer. The whole above-mentioned process is called rapid prototyping or 3D printing [12, 13]. **Figure 1** shows the formation process of a three-dimensional physical model.

There are various examples of the methods for producing a 3D sample by 3D printing technologies, such as Binder Jetting (BJ), Photopolymer jetting (PJ), Selective Laser Sintering (SLS), Fused Deposition Modeling (FDM). It is among these technologies. Among the different methods of making 3D samples, FDM and SLS are two common types of 3D printing technology which many researchers and manufacturers

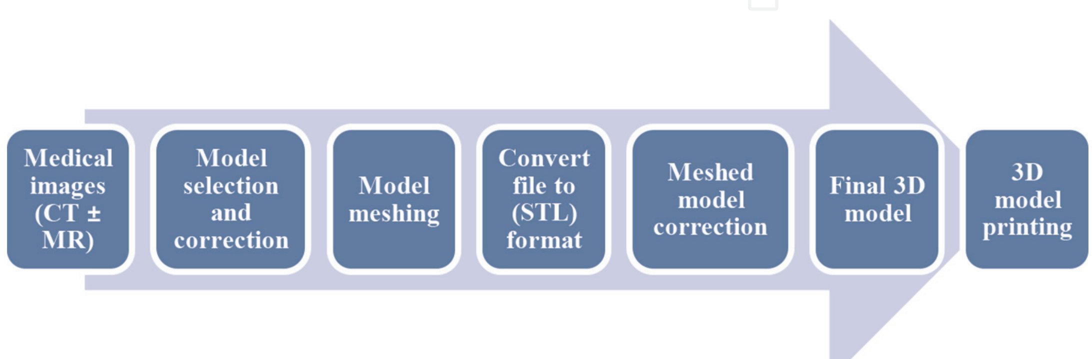

Figure 1.
The process of creating a 3D physical model using 3D printing technology based on medical imaging data.

have taken advantage of this method. One of the most famous 3D printers is the RepRap device [14].

Rapid advances in 3D printing technology have caused this technology to be increasingly used in the fields of medicine and health. In the field of medicine, this technology is used in the production of personal medical devices, implants, models for medical education, simulations, medical research, and also models for designing pre-operative treatment [11, 14].

3. Performed materials in 3D printers

So far, several materials have been used to produce the desired 3D object by the 3D printer, including polylactic acid (PLA), acrylonitrile butadiene styrene (ABS), polyethylene terephthalate glycol (PETG), thermoplastic elastomers (TPE), polyamide (PA also known as nylon), thermoplastic polyurethane (TPU), and polyvinyl acetate have been evaluated for use in radiation therapy [15, 16]. The success of 3D printing technology depends on the applied materials to create the desired 3D object [15]. The physical properties of the most important 3D printing materials are shown in **Table 1**.

PLA and ABS are two examples of the most common materials used in 3D printing technology [15]. PLA is a kind of odorless plastic polymers. This material is used in many industries, including degradable implants and food packaging. ABS has more resistance than PLA, and it is also resistant to high temperatures. As a plastic polymer, PA material is very resistant. In addition, it is flexible and very consistent. The most common application of TPE is in the construction of flexible objects, so that by using TPE, it is possible to create an object in a short time. PETG material is a combination of PET and glycols with different concentrations. Similar to PLA, PETG is used as a safe plaster for food containers and has been approved by the Food and Drug Administration (FDA). Compared to PLA, PETG is strong and hard. All the materials mentioned above are available in the form of filaments with diameters of 1.75 mm and 3 mm [15].

4. Applications of 3D printing technology in radiotherapy

Today, in spite of considering the tremendous advances in the radiotherapy, some radiotherapy steps are performed completely manually by the operator, therefore, a level of uncertainty is introduced in the clinical use of radiotherapy. Practical use of

Filament	Tension	Density	Flexibility	Durability	Printing problem	Printing temperature (°C)
ABS	Medium	1.01	Medium	High	Medium	210–250
PLA	Medium	1.24	Low	Medium	Low	180–230
PETG	Medium	1.27	High	High	Medium	220–235
TPE	Low	—	High	Medium	High	225–235
Nylon	High	—	High	High	Medium	220–260

ABS: acrylonitrile butadiene styrene; PLA: polylactic acid; PETG: polyethylene terephthalate glycol; TPE: thermoplastic elastomers.

Table 1.
Physical properties of 3D printed materials.

3D printing technology in radiotherapy can improve treatment results and reduce treatment errors. Recently, in the field of radiotherapy, the creation of objects from CT and MRI imaging data for various applications using professional and conventional 3D printers has been investigated by several groups of researchers. The main applications of this technology in radiotherapy, as shown in **Figure 2**, include making patient-specific blouses, fixation devices, brachytherapy applicators, compensation blocks, quality assurance phantoms, filters and grade blocks are therapeutic.

4.1 Radiotherapy bolus

In radiotherapy, one of the most common applications of 3D printing is the production of patient-specific bolus. So far, many studies have been done in the field of 3D printing to produce special blouses (**Figure 2E**). Bolus is a synthetic substance that is placed on the surface of the treatment area to correct the dose at the surface and depth of the skin, which can be used in both photon and electron beam radiotherapy [16]. Radiotherapy boluses can be created from commercial materials such as synthetic gel sheets, wet gauze, wax and thermoplastic sheets [22]. The preparing boluses methods are based on wax and thermoplastic materials is completely manual, which involves the level of uncertainty in its creation and use. In addition, the mismatch between the level of the bolus and the patient's level can lead to the creation of air cavities, which itself leads to a dose difference between the treatment plan and the dose delivered to the patient [16, 23–26].

Today, 3D printing technology provides the manufacturing of patient-specific bolus, so that it can lead to improved uniformity and dose distribution on complex and irregular surfaces [16]. It has been established that the 3D printed boluses used at the bedside can optimize the treatment preparation time and reduces costs of manufacturing process [27]. Besides, it has been shown that the use of this technology to create a bolus is safe and practical which also increases the work efficiency while increasing the quality of radiation dose delivery [27].

Park et al., have been used 3D printing technology to make a blouse for a 45-year-old man with Kimura disease who had received several sessions of radiation. Placing the 3D printed bolus in the treatment area placed the target position at an acceptable level and the air gap between the patient's body and the bolus was less than 5 mm. Most of the desired area was covered by a 3D printed blouse with a 95% uniform dose

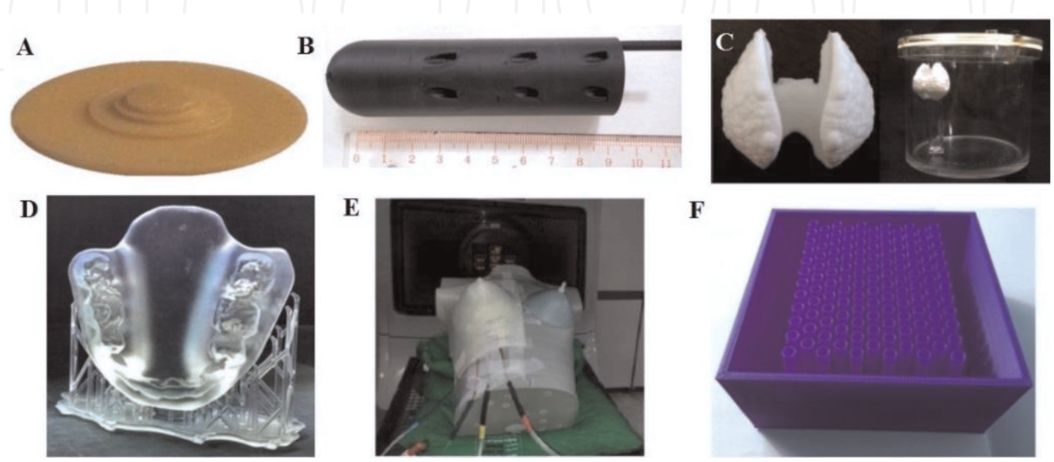

Figure 2.
3D printer filter (A), brachytherapy applicators (B), phantom (C), oral stent (D), blues (E) and block grade therapy (F). Adapted with permission from references [15, 17–21].

curve. Finally, the results of 3D printed boluses compared to the non-bolus state and even with paraffin wax blouse led to the improvement of the treatment target coverage [28]. The clinical effectiveness of bolus in head and neck cancers, head angiosarcoma, and after mastectomy has been investigated in many studies [29–31].

The presence of an air gap between the bolus and the patient's body has a significant effect on surface doses which can lead to a skin dose reduction [32, 33]. Fujimoto et al. designed a 3D bolus for the patient using CT images data. After placing the 3D printed bolus on the phantom, the results of dosimetry showed that the use of this special bolus can reduce the air gap and facilitate the dose coverage of the studied volume [34]. Besides, Ricotti et al., determined the dosimetric properties of common applied materials of ABS and PLA as printing materials that are usually. In this study it has been showed that the different filling percentages of these two substances lead to the creation of different densities, which can lead to differences between the calculated and measured dose distributions [35].

4.2 Brachytherapy applicators

Another application of 3D printing technology is the creation of applicators in brachytherapy. Several studies have investigated the 3D printing patterns to produce specific applicators that accommodate to the anatomy of each patient during the brachytherapy. The feasibility of 3D printing mold in brachytherapy was determined by Harris et al. [36]. The results of their study showed that a low-cost 3D printer with ABS plastic can accurately produce specific mold structures and catheter channels [36].

Recently, the production of templates for skin cancer brachytherapy using a 3D printer has been reported, so that the 3D printed template has led to a reduction in financial costs and clinical workflow [37]. In head and neck brachytherapy, applications of 3D printed applicators for implanting radioactive iodine-125 can accurately transfer a CT-based treatment plan to the brachytherapy needle insertion process [38]. In addition, using a separate 3D printed template (to guide the brachytherapy needle) the time required to insert the needle can be reduced and minimized the complications associated with incorrect implants [38].

In Seki et al. study, two cases of personalized 3D printed templates which were designed inversely from CT or MRI data were investigated for interstitial brachytherapy for cervical cancers (**Figure 2B**) [18]. As investigated in other studies, the accuracy of 3D printed model was accepted at a high level [39, 40]. There are two main weaknesses in conventional brachytherapy applicators. First, inability of the adaptation to the anatomy of the patient's body which leads to a change in the operator's position in a treatment department. Second, daily repeatability based on the requester's situation is considered a challenging issue [12]. However, the use of inexpensive 3D printers is a promising solution for creating high-dose brachytherapy applicators [12]. Jones et al., have shown that 3D printed applicators can improve high-dose surface brachytherapy using pre-programmed catheter orientation [41].

4.3 Phantom construction

Phantoms are widely used for quantitative and qualitative evaluations in medical imaging and radiotherapy (**Figure 2C**) [12]. Recently, several studies of 3D printing technology for making phantoms have been reported [11, 42]. In Tino et al. study, a significant increase in the publication of articles during the last 10 years in the field of imaging and dosimetry phantoms produced by 3D technology (number of 52 articles) has been reported. One of the main features of 3D printing technology was the production of customized additives and the possibility of density variations [43].

In medical imaging, researchers investigated the feasibility of an anthropomorphic chest phantom produced with a 3D printer for medical imaging purposes. Using 3D printing technology, they created a phantom based on the CT image taken from the chest of a patient with lung cancer. The phantom printed by 3D technology was examined in terms of size, shape, and structure by PET scan and CT scan. The results of the investigation showed that the phantom is able to withstand radiation doses of more than 24,000 Gy [7]. Today, many 3D printers produce 3D images of human organs [15]. 3D printing technology enables researchers to produce commercial phantoms and organs in a cost-effective manner compared to commercially available phantoms. Recently, several studies have reported that the use of 3D printing technology can create phantoms with variable density to ensure the quality of radiation therapy [6, 44]. 3D printing provides an inexpensive way to design and manufacture phantoms [45]. Also, the feasibility of 3D printed phantom for in-body artificial dosimetry in ensuring the quality of IMRT before treatment was examined. The results showed that the dose difference between the anthropomorphic head phantom and the 3D printed phantom was generally less than 2% [46]. In another study, to verify the accuracy of CyberKnife Xsight Lung Tracking System (XLTS) compared to Fiducial-based target tracking system (FTTS), a lung phantom made by 3D technology was used. XLTS and FTTS are Synchrony's two real-time respiratory tracking systems in CyberKnife robotic surgery. 3D printing technology has a very good ability to create lung phantoms [47]. It has been suggested that in the future multi-material printing using polymer jet technology will be used as an important printing process with the ability to create heterogeneous phantoms for dosimetry in radiotherapy [43].

4.4 Stabilizer devices

Recently, several advanced radiotherapy methods such as SBRT have been clinically used. In these techniques, accurate adjustment and immobilization of the patient is very crucial to ensure about the optimal dose coverage of the target volume and preservation of healthy tissues [44]. For this reason, immobilization of the patient is essential, especially in the head and neck area due to the tumor is usually located in the vicinity of endangered organs such as the brain stem or the spinal cord [48].

Nowadays, thermoplastic masks are usually used to immobilize the patient body [49]. Other immobilization devices include stereotactic frames, Scotchcast masks and bit blocks [44]. The most important concern about fixation devices can be attributed to the accuracy of fixation during the treatment session as well as different treatment sessions. In addition, the head mask can lead to physical discomfort and claustrophobia in some patients [50, 51]. Generally, it is necessary to improve the comfort of fixed devices in order to provide the best coverage and the least discomfort for the patient. Recently, a few studies have focused on the printing of fixation devices based on the anatomy of each patient by 3D printing technology.

In Haefner et al. study, a new method for making head fixation devices according to individual anatomy with 3D printing technology based on MRI data has been introduced. In this study, eight volunteers were studied and the 3D MRI data obtained from the head was processed using software and a meshed model of the surface of the fixing mask was obtained. Then, a fixing mask for the head was produced by a 3D printer and ABS material. The results showed that there is a high level of adjustment precision and also the patients had the least discomfort during use [44].

Besides, an oral stent was used during head and neck radiation therapy to reduce the side effects of radiation to healthy tissues. When an oral stent is used, the normal tissue is moved away from the high dose areas. Normally, the dentist makes an oral stent based on the image of the patient's teeth and a model of the relationship between the upper and lower jaw. The main purpose of using an oral stent is to increase the level of confidence and place the jaw in a reproducible position during radiation therapy. Nevertheless, there are various problems in using this device, among which it can be mentioned that it is difficult and time-consuming [20]. Recently, a new method for creating a patient-specific oral stent from common CT imaging data and 3D printing technology has been described by Wilke et al. (**Figure 2D**). Oral stent production using 3D printing method does not require the physical presence of the patient and will lead to a reduction in treatment time [20].

In Asfia et al. study, the result of published articles from 2000 to 2019 in the field of 3D printer fabrication of stabilizers was reviewed. The results of this study showed that with the advent of 3D printing technology, the manufacture of stabilizers by 3D printer is more affordable and accessible, so that functional parts They are able to produce more. Also, in this study a favorable agreement of the fixators in terms of matching the unique body geometry of the patient and also the possibility of repeatable adjustment for treatment have been reported [52].

4.5 Other applications of 3D printing technology in radiotherapy

In addition to the applications of 3D printing technology in above mentioned radiotherapy advances over the past few years, few studies have used 3D printing technology to make individual-oriented, compensating, and block grid radiation therapy filters [16, 17, 53, 54]. Filter production based on the individual characteristics and anatomy of the patient is considered an essential factor. Creating a filter is very time-consuming and its widespread use has not been reported [55, 56]. In this regard, a new method for creating special filters for the formation of electron beam fields using 3D printing technology has been described (**Figure 2A**) [17].

A very useful treatment method for large tumors is spatially fractionated radiotherapy (SFRT), which uses a special block to create a grid-like pattern. Grid therapy is an effective method for treating large tumors. Although radiotherapy with grade is effective, the clinical application of this method is limited due to inadequate understanding of radiobiological mechanisms [57, 58]. In addition, it is time-consuming and difficult to make specialized blocks that create radiation beams in the form of a network.

Today, the use of 3D printing technology can solve the limitations of access to specialized blocks in grid therapy. In 2015, Zhu et al. investigated cerrobend networks and used a three-dimensional technique for radiation modulation to create them (**Figure 2**). The block grid template was designed with tubes that lead to beam divergence. The mold was printed by a 3D printer using resin at a temperature of less than 230°C. Cerrobend liquid was melted at 120°C and poured into a resin mold and prepared for a block with a thickness of 7.4 cm. By using a small field dosimeter including a pinpoint ionization chamber and a stereotactic diode, the dosimetric characteristics of the grid block were investigated. For the 6 MW photon beam, the valley-to-peak ratio was 20% at dmax and 30% at a depth of 10 cm. The output factor was 84.9% at dmax and 65.1% at a depth of 10 cm. Their study showed that the 3D printing method can be used in grid therapy [21].

Another application of 3D printing technology in radiotherapy is the creation of compensatory blocks in IMRT [52]. Multileaf collimators and compensating blocks are two basic techniques used to modulate the intensity of photon beams. The conventional method of making IMRT compensating blocks is the use of milling machines, one of the disadvantages of which is the high operating and production cost compared to the lead multi-leaf collimator method. To eliminate the need for milling machines, 3D printing technology has been used to make IMRT compensatory blocks. The main advantage of this approach is reducing costs and production time [53].

5. Conclusion

The use of 3D printing technology will reduce the cost of radiotherapy, and as a promising method, it can lead to the treatment of cancer in a specific and person-centered way. Studies conducted on 3D printing showed that this method is a fast, practical and inexpensive method to deliver a uniform dose to the target volume and at the same time protect healthy tissues in the radiation field. In addition, this technology reduces the patient's discomfort and provides special radiation therapy devices suitable for each patient.

In this chapter, the main applications of 3D printing technology in radiotherapy in the manufacture of special treatment devices such as bolus, phantom, brachytherapy applicators, filters, patient fixation devices, compensatory blocks and grid blocks. There are various materials for 3D printing that can be used for better delivery of radiotherapy. The use of 3D printed devices based on the anatomical features of each patient in radiotherapy, such as bolus and fixing devices, can reduce daily uncertainty and also increase the accuracy of treatment.

The conducted investigations showed that patient-specific devices can be produced by 3D printing from volumetric CT images or MRI data. In practice, 3D printing technology has a great potential to improve accuracy and efficiency in the field of personal radiotherapy. 3D printing technology offers a relatively low-cost and effective way to produce devices based on individual anatomy in radiotherapy. When a new technique is introduced at the bedside, it is necessary to develop appropriate quality assurance programs to protect patients and healthcare professionals. Further developments in the field of 3D printing technology can create more flexibility in design, so that this method can be applied to the bedside as well. Besides, new 3D printing materials and methods that lead to better results in the treatment of patients will be introduced in the not-so-distant future.

Abbreviations

IMRT	Intensity Modulated Radiation Therapy
IGRT	Image Guided Radiation Therapy
SRS	Stereotactic Radiosurgery
SBRT	Stereotactic Body Radiation Therapy
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
STL	STereoLithography

BJ	Binder Jetting
PJ	Photopolymer jetting
SLS	Selective Laser Sintering
FDM	Fused Deposition Modeling
PLA	polylactic acid
ABS	acrylonitrile butadiene styrene
PETG	polyethylene terephthalate glycol
TPE	thermoplastic elastomers
PA	polyamide
TPU	thermoplastic polyurethane
FDA	Food and Drug Administration
SFRT	spatially fractionated radiotherapy

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