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Research Article

Personalized Intraoperative Radiotherapy Balloon Applicator Design and Production With 3D Printer

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Abstract:

Radiation is the energy released from matter. Radiation is divided into two according to its source: natural and artificial radiation. Artificial radiation is used in treatment methods in medicine. One of these treatment methods is brachytherapy. Brachytherapy treatment is applied by placing small radioactive sources inside the body and sending beams directly to the cancerous cell. The main thing to consider in brachytherapy treatment is the selection of the applicator. The applicator is the device that enters the patient's body cavity. In this study, based on the applicators currently used in the medical field, a patient-specific, biocompatible, sterilized, and reusable applicator will be created from PLA material by using a 3D printer. The applicator to be designed will consist of 2 parts: the intrauterine tube and the spherical tip. The spherical tips, which vary according to the size of the tumor, will be pressed to integrate with the tube part of the applicator. Thus, a patient-specific design will be realized by using the spherical tip suitable for the patient's tumor region. As a result of the project, since the applicator will have spherical tips of different sizes, it completely covers the intrabody cavity of the patient. Thus, the movement of the applicator is limited, and dose distribution is prevented. The treatment process of the patient is improved. Another result is that the prototype applicator printed with PLA filament is produced at a very low cost. Thus, access to the applicator becomes easier and its use in the medical field increases.

1. Introduction

1.1 Radiation

Today, radiation is a concept that we frequently encounter in our environment. Radiation is the energy released from matter. Physically, it is the propagation of various types of energy in waves [1]. According to energy and frequency level, radiation is divided into two main categories: ionizing and non-ionizing. Ionizing radiation creates ions in the material it hits, and energy is transferred by electron detachment from this ion [2]. It is also referred to as nuclear radiation. The type of radiation used in the medical field is ionizing radiation. They have high frequency, low wavelength, and damage tissues due to their high energy. They have the energy to break down the DNA inside the cell as a result of uncontrolled exposure. Due to the damage to DNA, it causes many diseases in the body, including cancer [3]. Non-ionizing radiation is ultraviolet rays, visible light and infrared rays, microwaves, and radio frequency that do not ionize the environment [4]. In this type of radiation with low frequency and high wavelength, ionization does not occur. In contrast to ionizing radiation, non-ionizing radiation does not have the energy to detach electrons from molecules. Therefore, it is not directly harmful to the human body. However, continuous exposure to high doses of non-ionizing radiation can damage the tissue due to the heat emitted.

There are many sources of radiation energy. The sun, radioactive materials, medical devices, and X-rays are some of these sources. These sources can be analyzed into two categories: natural and artificial. Natural radiation is the radiation that exists in nature without human contribution. The main headings of natural radiation can be grouped as cosmic, terrestrial, and internal radiation [5]. The radiation we are exposed to from the sun, stars, Earth, rock, soil, water, and air, and the types of radiation naturally found in the human body (Potassium-40/ Carbon-14 isotopes) are examined under this heading.

Artificial radiation sources can also be divided into two as medical sources and industrial products. Since there is no continuous exposure like natural sources, exposure may vary depending on the person's daily lifestyle. Medical sources are the area of use of ionizing radiation. It is the type of radiation exposure due to medical diagnosis and treatment areas such as radiography, radiotherapy, and nuclear medicine [5]. In radiography and imaging methods, low doses of radiation are used for diagnostic purposes without harming the cells and the patient. However, since apoptosis occurs in radiotherapy, high doses of radiation are targeted.

While radiation can be extremely harmful to the human body, it can also be beneficial. For example, while it can cause cancer as a harmful effect, at the same time, cancer can be cured with radiation used in the appropriate dose and area. For this reason, to use the effects of radiation correctly, an appropriate and controlled dose should be selected, and the duration of exposure should be adjusted correctly. Measurement units are used internationally to adjust this dose correctly and to obtain reliable results in studies.

The number of decays of radioactive nuclei per unit of time is known as activity and its unit is Becquerel (Bq) [6].

The amount of radiation energy stored as energy due to ionization in the environment is the absorbed dose. The unit of this dose is Gray (Gy) [7].

Stochastic and deterministic effects may occur if radiation is not used at the appropriate dose and duration. These effects are extracellular effects. Deterministic effects are the effects when radiation damages a tissue or organ, and the body reacts. There is a certain threshold value and if a dose smaller than this threshold value is received, the effect is zero. However, if radiation is received above this threshold, damage occurs in the body. The damage increases depending on this dose. The most common effects are infertility, sudden death, and cataracts. For example, cataracts can occur with 5 Gy or more radiation to the eye [7]. Stochastic effects are those observed without any threshold value. They occur as the effects of low doses of radiation. Their effects are not sudden like deterministic effects but are observed later. Here the damage/ threshold connection is linear. The more exposure to radiation, the greater the damage/ disease that will develop [7].

1.2 Use of Radiation in Healthcare

Radiation is used in various fields of health such as diagnostic imaging and radiation therapy. It is important to use radiation safely and appropriately to minimize health risks. There are various radiation devices used for different purposes in healthcare. Some of the radiation devices used in healthcare include X-rays, CT, PET, MRI, and radiotherapy. X-rays provide imaging of the internal structures of the body using ionizing radiation with X-rays. Computed tomography (CT) provides detailed imaging of the body using ionizing radiation and is used to diagnose internal injuries and diseases by combining X-ray images taken from different angles [8]. Positron Emission Tomography (PET) provides metabolic and functional imaging using a radioactive tracer injected intravenously. Magnetic Resonance Imaging (MRI) uses magnets to emit magnetic fields and radio waves to create images of the body. Radiotherapy uses high-energy radiation to target and destroy cancer cells. There are different radiation therapy machines. These include beam radiation therapy, brachytherapy, and proton therapy.

These devices play an important role in the diagnosis and treatment of diseases. With the right radiation used in the health field, early diagnosis of diseases, non-invasive treatments and a more comfortable treatment process for the patient can be realized. Radiation doses should be monitored and minimized to reduce harmful effects due to the radioactive effects of the devices.

1.3 Radiation and Radiotherapy in Cancer

Cancer is a disease caused by the uncontrolled and irregular growth and division of cells in the body [9]. During this uncontrolled growth process, the cells cause great damage by damaging the healthy tissues around them.

The most common types of cancer are breast cancer, cervical cancer, colon cancer, and prostate cancer. Risk factors include genetic factors, age, and environmental factors.

Early diagnosis makes cancer treatment more effective. However, the treatment process may vary depending on the stage and type of cancer. There are different treatment methods such as chemotherapy, surgery, and radiotherapy. Almost 50% of cancer patients receive radiotherapy [10].

Radiotherapy is one of the most common treatment methods [7]. While its main purpose is to destroy cancer cells using high-energy radiation beams, it can also be used to shrink cancerous tissue and relieve symptoms. These beams are directed directly at the cancerous cells, causing damage to the structure of the cancerous cell, and slowing/ stopping the cancer. The duration and dose of treatment is determined depending on the patient and the course of the disease.

The radiotherapy method may also change according to the course of the disease. The most used radiotherapy methods can be explained as follows. In EBRT (External Beam Radiation Therapy), high-energy beams are used for cancerous cells. The machine with the radiation source rotates around the patient, focusing the beams on the cancerous cells. IGRT (Image Guided Radiation Therapy) uses imaging techniques to directly target the cancerous area. The most common imaging techniques in this method are CT and MRI. Since the area is directly targeted, radiation can be directed more accurately. Tomotherapy treatment is one of the most common IGRT methods. Dosimetric planning is provided with 3D imaging. Another method is intraoperative radiotherapy.

1.4 What is Intraoperative Radiotherapy?

The word brachytherapy is a combination of the Greek words $brachy + therapy$, which means short distance + treatment [11]. In this method, the radioactive material is placed in direct contact with the cancerous cell and inside the cancerous tissue, exposing the tissue to radiation. It is applied after the removal of cancerous tissue during surgery [12]. Cancerous tissue cannot be completely removed from healthy tissue when surgically intervened. As explained in the previous section, the effectiveness of the treatment is quite high in this method since IORT directly contacts the cells intensively. For the same reason, the damage caused by IORT to healthy tissue is also minimal [12].

The radiation sources used in this method are high-energy x-rays, electrons, and gamma rays. Since breast, pancreatic, uterine, head, and neck cancers are more prone to spread, IORT is highly utilized for these cancers [13].

Unlike conventional radiotherapy, IORT delivers a higher dose of radiation to cancerous tissue while at the same time protecting healthy cells more [14]. This reduces the duration of the patient's treatment [15]. Due to the protection of healthy cells, side effects can be observed less frequently.

It is applied with a device placed in the tissue after surgery. Electron radiation has a limited range and thus causes less damage to surrounding tissues. Gamma rays are applied to the tissue with a special device. It provides a more homogeneous radiation distribution compared to other radiation methods.

As a result, the choice of method for IORT should be carefully and meticulously selected in light of the patient's condition, the course of the disease, and the doctor's attention [16]. IORT, which offers highly effective treatment in a short time, is costly due to the devices, heads, and other external factors used. In addition, the fact that the applicators used to directly contact the tissue and destroy the cancerous area are compatible with the patient will increase the effect of the treatment. Thanks to the applicators we have discussed and designed in this study, we aim to increase the preference and effectiveness of the treatment result by reducing the cost and increasing the patient compatibility of the applicators.

2. Material and Methods

In order to print the prototype applicator, which we expect to be used in the brachytherapy method, using an FDM type 3D printer, a product design was made in 3D space with the Autodesk Fusion 360 program. In the product design, the Axxent electronic applicator, which is used in the literature for breast cancer treatment, was used as a template for the drawing, inspired by the studies in the literature. The product designed is made up of two main parts, the applicator tube, and the spherical tip.

The spherical tips, which vary according to the size of the tumor, were 3D printed to integrate with the tube part of the applicator. Spherical tips, which provide patient-specific applicator design and differ in size from each other, were developed in accordance with the patient's tumor region. The tube part of the applicator, unlike balloon applicators, contains only a port suitable for radiation entry. Produced in accordance with the use of Ir-192 high dose rate (HDR) radiation source and/ or electronic x-ray source, the applicator transmits the radioactive material from the radiation port to the spherical tip. The two-piece prototype applicator was turned into an object by on a printing on 3D printer, using PLA polymer material which is a commercially available inexpensive, biocompatible, and high-resolution filament.

3. Results and Discussions

Devices for creating three-dimensional objects from digital designs are called 3D printers. 3D printing can be defined as the process of creating objects by adding the material used layer by layer. Therefore, production in 3D printers is an additive process. It is formed by the combination of layer sections at the specified resolution [17].

Designs for 3D prints can be easily edited and reprinted, allowing test-based optimization. Additionally, 3D-printed devices do not require a cleanroom fabrication environment. Consumables for 3D printing are usually just resin and solvent to remove support materials, so costs can be low [18].

Various types of 3D printers are available on the market, including Fused Deposition Modelling (FDM), Stereolithography (SLA), Digital Light Processing (DLP), and Selective Laser Sintering (SLS). FDM 3D printers, which operate by heating and extruding a plastic filament to form an object, are the most popular and affordable type of 3D printers. To form an object with FDM, the filament is melted and extruded through a hot tip nozzle moving in the x, y and z axes, and the molten filament is deposited layer by layer. In other words, the basic concept of the FDM manufacturing process is simply to melt the raw material and shape it to create new shapes. The material is fed through a nozzle placed on a roller, pulled by a drive wheel, and then temperature controlled.
It is a filament that is put on the head and heated until it becomes semi-liquid [19]. FDM 3D printers are frequently used in prototyping, manufacturing, and product design work. In addition, FDM printers can print with various materials such as PLA, and PETG, which are easily available in the market. These features also make them useful.

FDM 3D printers, which create objects by depositing melted filaments layer by layer, create objects using various filaments. The filaments used are mainly PLA (Polylactic Acid), PETG (Polyethylene Terephthalate Glycol), Nylon, TPU (Thermoplastic Polyurethane), ABS (Acrylonitrile Butadiene Styrene).

Although FDM-type 3D printers are compatible with working with many filaments, PLA is the most preferred filament due to its usefulness and cheapness. PLA filament is a widely used material for 3D printers. PLA is a naturally sourced, biodegradable, and environmentally friendly material and is often produced from natural raw materials such as corn starch. Polylactic Acid (PLA) is the most used thermoplastic and natural fibers can be used as a filler [20]. Biocomposite filaments consist of a biodegradable composite matrix and biofillers. Additives can make fibers or particles. Therefore, PLA is a popular thermoplastic material used in fusion deposition modeling (FDM) with a wide variety of medical uses [21].

PLA filaments are a type of thermoplastic material that melts when heat is applied and can be reshaped. PLA is suitable for high-precision printers and can be used to produce very precise parts. Made from renewable resources with a low melting point, biodegradable, biocompatible, low bending coefficient PLA filament allows users to create safe, good dimensional stability prototypes.

A good material for bioengineering is PLA. It has a wide range of medicinal applications, including orthopedic and dental purposes as well as tissue engineering and regenerative medicine. The advantages of this material have helped engineers and scientists [22].
It has minimal to no documented carcinogenic impact, and is easily manufactured, recyclable, biodegradable, and biocompatible [23]. Also permitted by the FDA for direct contact with biological fluids is PLA.

A method to exterminate all microbial life forms, such as viruses and bacteria, is referred to as sterilization [24]. Especially in the medical field, sterilization of these microbial life forms is of great importance as they are undesirable substances. Recently, with PLA being a frequently used material in medicine, studies have also been conducted on its sterilization and sterility in surgical use. Among these studies, hydrogen peroxide sterilization is the most suitable method for 3D-printed PLA materials. The sterilization with hydrogen peroxide prevents the deformation of 3D-printed PLA materials during autoclave sterilization [25]. With sterilization with hydrogen peroxide, the designed applicator can be used intraoperatively many times.

Depending on the molecular weight and degree of crystallinity of the polymer, PLA's mechanical characteristics can change [26]. With different PLA isomers and functional groups, these values alter. Table 1 lists the PLA's mechanical and physical characteristics. varied isomers and functional groups have varied values for these parameters.

Table 1. *Physical and Mechanical Properties of PLA [27]*

Properties	PLA
Polymer Density	1.21-1.25 g/cm^3
Tensile Strength	21.0-60.0 Mpa
Tensile Modulus	0.35-3.50 Gpa
Ultimate Strain	2.5-6%
Specific Tensile Strength	16.8-48.0 Nm/g
Specific Tensile Modulus	0.28-2.80 KNm/g
Melting Temperature	150-162 ºC

The most important factor to consider when choosing a polymer to utilize as a biomaterial is whether its mechanical characteristics and rate of degradation are appropriate for the application.

Physical features are also crucial for a medical device; therefore, the designer must take into account the product's dimensions, size, and weight specifications. For instance, the design should safeguard the product against weights, pressures, and impacts while yet being light enough for the surgeon to handle precisely [28].
Tensile strength, tensile elongation, tensile modulus, impact resistance (all for toughness), and flexural modulus are significant mechanical qualities.

Applications for PLA include tissue engineering, medication delivery systems, orthopedic and fixation devices, and wound care and stents. In one work, a polymer based on lactic acid was used to create an implantable decomposable inflated balloon [29]. By separating the prostate rectum with balloons during radiation treatment for cancer, or to cure severe rotator cuff injuries, it has been employed as a sub-acromial separator [30].

Various software programs are used for designing and prototyping 3D models. Software developed for Computer-Aided Design (CAD) allows users to create 3D models, simulate their designs, and prototyping by providing various features. Today, actively used, and popular software: Autodesk Fusion 360, SolidWorks, SketchUp, and Blender can be listed as.

Autodesk Fusion 360 is a design and manufacturing software. This software is designed for the design, simulation, manufacturing, and learning of products and offers a variety of design tools, simulation features, manufacturing features, and learning tools. Autodesk Fusion 360, a cloud-based CAD/CAM (Computer Aided Design/ Computer Aided Manufacturing) software, offers a host of features for designing and prototyping 3D models, including parametric modeling, sculpting, and direct modeling, as well as tools to simulate the performance and behavior of designed parts. allows users to test their designs before producing them. Thus, it is widely used in various industries including engineering, product design, and manufacturing. The fact that Fusion 360 is a cloud-based software prevents data storage in local memory, while project files can be accessed from anywhere with an internet connection. Another advantage is that it allows users to collaborate on projects in real-time.

In additive manufacturing, the slope of a downward-facing surface (protrusion) of the object is above a critical value relative to the base plate for the object to be self-supporting. If a part contains regions with projection angles below this critical value in the intended construction direction, it will not be self-supporting and cannot be printed as it is [31]. Therefore, the critical angle must be determined, and the design must be made accordingly. However, changing an optimized geometry can degrade the object's performance or even render it inapplicable. For this reason, it is a more preferred method to support the object with traditional supports and remove it from the object when the printing process is completed.
Thanks to the "overhang optimization" or "self-supporting structures" methods, balloon-shaped object output can be obtained without using support structures. In addition, these methods aim to reduce material waste and post-processing efforts. "Mesh Structures" and "Gradual Overhangs" are some of the techniques used for these methods. There is a special design on the basis of these methods. The use of supports can be minimized by using gradual angles and curves in the design.
In our study, the FDM type 3D printer PLA material is deposited layer by layer and the object comes out of the printer. This causes the resulting object to have a rough structure. In our study, sanding and polishing processes were carried out respectively to make the object smooth. Thanks to these methods, which are frequently used in the production of medical devices with 3D printers, the use of support can be minimized, and the created device can be smoothed.

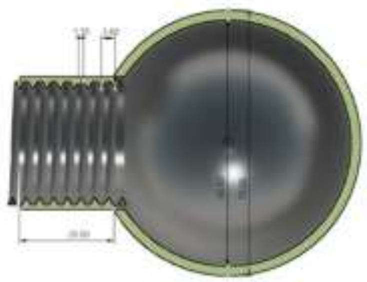

Figure 1. *Spherical Tip Sketch*

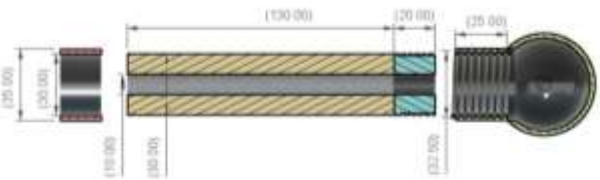

Figure 2. *Whole Applicator Sketch*

Figure 3. *Whole Applicator 3D View with Two Different Spherical Tips*

Figure 4. *Three Different Spherical Tips with the Radius Parameter*

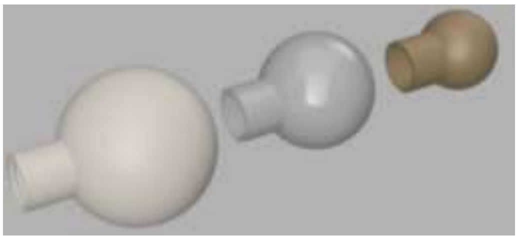

Figure 5. *Three Different Spherical Tips*

In the Figure 1, the spherical tip sketch made in Autodesk Fusion 360 is shown with the parameters. Figure 2 shows the whole applicator design with the applicator tube, and the spherical tip.

The general view of the applicator is shown in Figure 3. The tube and spheric type are shown in this figure with their external appearance.

Figure 4 shows the cross-section of the spherical tips. This figure shows the parameters and the cross-section of the tips with different diameters.

The whole view of the cross-sectional images given in Figure 4 can be observed in Figure 5. In this figure, the whole appearance of the tips with different radii is shown.

The design of the applicator to be used in the intraoperative treatment has been completed and its external appearance and drawings are given in the figures. Accordingly, applicators, which are drawn and printed according to different diameters, are expected to be effective for treatment in cases that vary according to different tumor sizes and the size of the patient's internal cavity. In addition, the applicator, which basically consists of two parts (tube and cylindrical tip), offers a simple solution for the use of paramedics and improves the treatment process based on the separate-clean-connect-use principle.

4. Conclusions

Traditional application methods and applicators used in brachytherapy treatment were examined in the literature. As a result of the literature review, the development process of the currently used applicators was examined and some deficiencies were revealed. The unique value of this study is the development of balloon applicators suitable for cervical cancer treatment using 3D printing and the creation of a sterilized and reusable applicator. The applicator to be created consists of two parts: a tube and a spherical tip. The spherical tips, which vary according to the size of the tumor, will be pressed to be integrated with the tube part of the applicator. Thus, a patient-specific design will be realized by using a spherical tip suitable for the patient's tumor area. The intrauterine tube will limit the movement of the biocompatible applicator to be produced, closing the gap in the tumor area, and facilitating access to the area to be exposed to radiation. This study will be one of the pioneering studies in the field and will be a reference for future studies. When compared with similar studies to be conducted in the coming years, this study will reveal the importance of applicators created with 3D printers for use in brachytherapy treatment in cervical cancer treatment.

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- **Ethical approval:** The conducted research is not related to either human or animal use.
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