

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



3D Printing Planning Stereotactic Radiosurgery in Uveal Melanoma Patients

Alena Furdova, Adriana Furdova, Miron Sramka,
Robert Furda and Gabriel Kralik

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.79032>

Abstract

The aim of our work is to use a new modality for visualization of intraocular tumors in three-dimensional space for planning of stereotactic radiosurgery procedure on linear accelerator. Malignant uveal melanoma is the most common malignant tumor of the inner eye structures in adults. Stereotactic radiosurgery on linear accelerator is the method of treatment that requires precise planning. However, in some cases, it is very difficult to imagine the structures based only on fusion of two-dimensional computed tomography (CT) and magnetic resonance imaging (MRI) scans. For the team of specialists planning the procedure, 3D printed models represent the way how to perceive the real shape of the tumor and its location considering the important structures of the eye globe. By using the open-source software for segmentation (3D Slicer), we created a virtual 3D model of the eye globe with a tumor that utilized tissue density information based on CT and/or MRI dataset. By creating and introducing a new imaging modality for tumor visualization, we provided real 3D model of the eye globe for the specialists that enabled them more effective planning of the stereotactic radiosurgery.

Keywords: fused deposition modeling, intraocular melanoma, stereotactic radiosurgery, 3D printer, 3D eye globe model

1. Introduction

Recent development of 3D printing enables to produce models of things, shapes, objects, and structures that before seemed more or less not possible to achieve. These technologies can

build a 3D object in almost any shape imaginable as defined in a computer-aided design (CAD) file. In a basic setup, the 3D printer first follows the instructions in the CAD file to build the foundation for the object, moving the head of the printer along the x-y plane. The printer then continues to follow the instructions, moving the head of the printer along the z-axis to build the object vertically layer by layer. It is important to note that two-dimensional (2D) radiographic images, such as x-rays, magnetic resonance imaging (MRI), or computed tomography (CT) scans, can be converted to digital 3D print files, allowing the creation of customized anatomical and medical structures [1].

Charles Hull invented 3D printing, which he called “stereolithography,” in the early 1980s. Stereolithography uses the “.stl” file format to interpret the data in a CAD file, allowing specific instructions to be electronically communicated to the 3D printer. Along with dimensions, the data in the “.stl” file may also contain additional information for 3D printer such as the color, texture, and thickness of the object. Hull later founded the company 3D Systems, which developed the first 3D printer, called a “stereolithography apparatus.” In 1988, 3D Systems introduced the first commercially available 3D printer, the SLA-250. Many other companies have since developed 3D printers for commercial applications. Hull’s study, as well as advances made by other researchers, had revolutionized manufacturing, and it was applied in many other fields, as well as in medicine research and practice [2].

Nowadays, many of 3D printing processes are available, and all of them offer advantages and disadvantages. The model of 3D printer selected for an appliance depends on the material types that should be used, and it depends on the required layers in the finished model they are supposed to be bonded. The used 3D printing technologies within medical applications are: selective laser sintering (SLS), thermal inkjet (TIJ) printing, and fused deposition modeling (FDM).

1.1. Selective laser sintering

An SLS printing technology uses as a substrate for printing new objects, a powdered material. The laser renders the shape of the object into a single layer of powder bonding the powder particles together. Then, a new layer of powder is laid down and the process repeats on and on, building layer by layer to form the object. Selective laser sintering can be used to create metal, plastic, and ceramic objects. The accuracy of the laser and the fineness of the powder material are limited by the degree of detail. This detail enables to create especially detailed and delicate structures, like the eye globe and its structures (lens, optic disc).

1.2. Thermal inkjet printing

Thermal inkjet printing is a “noncontact” technique that uses piezoelectric, thermal, or electromagnetic technology to deposit tiny droplets of ink or other materials that are used onto a substrate according to digital instructions. Heating of the head of the printer creates small air bubbles that collapse and create pressure pulses that eject ink droplets from nozzles in

volumes from 10 to 150 picoliters. Droplet size can vary by adjusting the applied temperature gradient, pulse frequency, and viscosity of the ink.

1.3. Fused deposition modeling

FDM printers are less expensive and more common than the SLS type. An FDM printer uses a head of the printer that is similar with an inkjet printer. However, instead of ink, as the printer's head moves, beads of heated plastic are released and build the object in thin layers. This process is often repeated, allowing precise control of the location and amount of each deposit to shape each layer. Since the plastic is heated as it is extruded, it bonds or fuses with the layers below. As each layer of material cools, it hardens and creates the solid object as the layers build. Depending on the complexity and cost of an FDM printer, it may have features such as multiple heads of the printer. FDM printers can use a variety of plastics [3].

2. 3D printing in ophthalmology

3D printing was introduced to medicine at the beginning of this century, when the technology was first used to create dental implants and individualized prosthetics. Since then, the medical applications for 3D printing technology have progressed significantly. The first published reviews describe the importance, utilization and results of 3D printing when applied in the field of orthopedic surgery, cardiovascular surgery, and tissue engineering, as well as in pharmaceutical development (new dosage forms, delivery of medicines, etc.). The current medical application of 3D printing technology is classified into several groups, such as prosthetics, implantation, and precise anatomical models; production of tissues and organs; and research in pharmaceutical industry on drug discovery, design of dispensers, and drug dosage forms [4].

2.1. 3D printing for eyewear and medical devices

3D printing technology has progressed to the point when companies print custom-made eyewear with their own design and on demand. The market for customization of eyewear has been made possible by a rapid prototyping. 3D printing enables and simplifies on demand production of medical devices in plastic or metallic form, and in the future, may represent the best way to produce artificial lenses, glaucoma valves and other personalized implants.

2.2. For education and clinical practice

3D printed models are already used in institutions for medical education—due to their accurate visualization are being used to introduce surgical techniques to trainees, young doctors or students before they start to treat patients. Surgical simulations using 3D models

allow students to practice in a safe environment, until they can perform the techniques at the expected level. Hypothesis that these models can shorten the learning curve, standardize training and assessment, became true. The results show that trainers using 3D printed models have done a lot to finish their tasks better and have a better learning experience than those who used only digital models or textbooks. This suggests that using 3D models enhances the understanding of anatomical structures, their collocations, and their relationships. With the advancement of 3D printing technology, the 3D print models can be made available to improve the training of young ophthalmologists in a simulated operating theater environment, thus improving the training experience.

2.3. For printing of live cells, tissues, and organs

The development of 3D bioprinting technology, including the printing of living cells, different tissues, and even organs, is now becoming an important and expanding field of medical research. From 2012, this technology has been studied in academic circles and by biotechnology corporations (e.g., Organovo Co., San Diego, CA, USA) for possible use in tissue engineering applications, where tissues and organs are created by using 3D inkjet printing technology. The technology process is based on placing living cells onto a gel medium or sugar matrix and layer-by-layer predefined 3D structures are formed. In this way, blood vessels, bones, ears and other structures can be printed. Using 3D bioprinting technology in 2014, researchers successfully implemented a 3D skull component into a patient, with no adverse effects. This new technology represents an extension of the treatment options for creating and adapting personalized implants to the patient. The use of three-dimensional bioprinting in ophthalmology is, however, still limited, but for the generation of ocular tissues (e.g., conjunctiva, sclera, and corneas), the use of 3D bioprinting technology in the future has a great potential.

2.4. For surgical planning

In the first place, the ophthalmologist must comprehend complicated anatomical structures of the eye globe and orbit and their connection with the suspected lesion. Structural relationships observed and defined between orbital structures, muscles, vessels, and nerves can be difficult to assess fully during the planning of the orbital surgery, based solely on the 2D scans obtained. The small surgical access field for eye globe (diameter 24 mm) also means that any mistake in navigating in this structures and complicated anatomy can have potentially devastating consequences for the patient—postradiation complications. Experience proves that, for both practical and educational purposes, the creation of an anatomically personalized organ models by using 3D printing technology is very useful. This technology allows a full appreciation of anatomical relationships and collocation between tumors or lesions and other complicated surrounding, but healthy structures. Advances in 3D printing technology enable the real prototyping of various anatomical structures and allow accurate representation of the patient's current state. In surgical or irradiation planning schemes in human medicine, it will be an invaluable aid to have this real 3D organ models.

It will provide a better possibility and learning experience for the doctors, physicists and surgeons [4].

We introduced the 3D printing technology into a process of planning stereotactic radiosurgery (SRS) in patients as a treatment of intraocular tumor—uveal melanoma [5, 6].

3. Intraocular melanoma

3.1. Definition

Intraocular melanoma is a quite rare type of cancer and is a disease in which tumor cells are formed in the part of the eye globe called the uvea (iris, ciliary body and choroid). Intermediate layer of the eye globe (uvea) contains melanocytes. Process of melanogenesis leads to produce melanin (can be found also in hair and in skin).

There are some cases in which doctors have detected intraocular melanoma during a routine eye globe examination. The chance of recovery depends on factors such as the size and cell type of the tumor. In support of classification, the staging system tumor node metastasis (TNM) is used for standardization of the tumors so the care teams can summarize information about how a tumor has spread. The information about the TNM classification is combined by a process called stage grouping. For example, intraocular melanoma grade T4 (due to classification) spreads to the orbit and extraocular tissues.

Uveal melanoma is relatively rare type of cancer, but the most common and most aggressive type of intraocular tumor in adults. The incidence of intraocular tumors varies from 0.2 to 1.0. Uveal melanoma mostly occurs in middle-aged people [7, 8].

3.2. Signs and symptoms

Most people with intraocular melanoma experience no symptoms of the disease in its early stages.

As the disease progresses, the following signs and symptoms can be seen:

- A growing dark spot on the iris.
- Change in the size or shape of the pupil.
- Problems with vision (blurry vision or sudden loss of vision).
- Floaters (spots or squiggles drifting in the field of vision) or flashes of light.
- Visual field loss (losing part of your field of sight).
- Increased intraocular pressure (secondary glaucoma).
- Change in the way the eye globe moves within the socket.

Only in cases when there is a massive spread outside of the eye globe, there may be pain. If someone has any of the symptoms above, it is important to visit a doctor immediately so the cause can be found and treated.

3.3. Localization of uveal melanoma

The localization of uveal melanoma is defined based on the area where the tumor is found in the eye globe and optionally based on the size of the tumor. The main localizations of the intraocular melanoma include the following tumors due to anatomical localization:

- Melanoma of the iris.
- Ciliary body melanoma.
- Choroidal melanoma (**Figure 1**).

In certain cases, intraocular melanoma can be complicated by extraocular extension. The most frequent metastases of uveal melanoma are in the liver.

3.4. Diagnostic methods

Slit lamp examination, ophthalmoscopy and fundus photo documentation are basic examination methods.

Melanomas from choroidea can vary from dark pigmented to amelanotic, some even partially pigmented. Small choroidal melanomas are characteristic with a typical shape, where the mass under the retinal pigment epithelium is nodular, dome-shaped and well-defined. During the growth of choroidal melanoma, more irregular configurations and shapes, such as bilobular, multilobular or spongy are observed. Diffuse choroidal melanoma, whose lateral growth in choroids with minimal elevation is a characteristic feature, it is more difficult to make a diagnosis. In many cases, the diffuse choroidal melanoma causes significant exudative retinal detachment.

If the tumor is lightly pigmented, then its abnormal vascularization can usually be detected by ophthalmoscope. Excessive choroidal melanomas usually cause changes in the epithelial

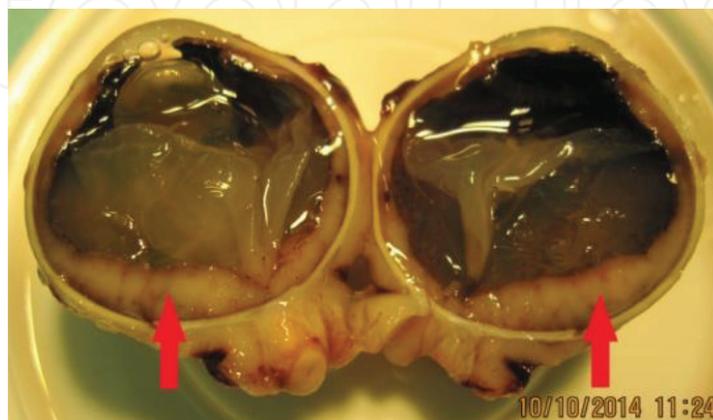


Figure 1. Enucleated eye globe with intraocular tumor—arrows shows the tumor mass (choroidal melanoma).

pigment of the retina (e.g., drusen), atrophy patches and orange color change. These changes can occur not only in malignant but also in benign lesions. Choroidal melanoma may remain undetected under a great exudative retinal detachment or subretinal or vitreous bleeding.

A rare occurrence of advanced choroidal melanoma results in a painful blind eye globe with cataracts and proptosis, resulting from tumor transscleral orbital enlargement. In anterior choroidal melanomas, sentinel vessels (dilated episcleral vessels visible through the conjunctiva) that nourish the metabolically active tumor may occur. Transscleral growing of the anterior choroidal melanoma (predominantly via the emission channels) can be identified during the examination as a small subconjunctival area of abnormal hyperpigmentation.

3.4.1. Ultrasonography

In the case of eye globe tumors having a diameter greater than 2–3 mm, A-scan ultrasonography is suitable for diagnosis. The choroidal melanoma scan depicts a characteristic initial prominent spike, followed by low to moderate internal reflection with decreasing amplitude and significant echo. Vascular pulses can be seen as fine oscillations of the internal spiking model in the tumor area. Standard ultrasonography, currently used, has a diagnostic accuracy of more than 95%. Performing sequential A-scans with accurate dimensional measurements is a recommended complementary method after uncertain outcome of primary diagnostics.

B-scan ophthalmological ultrasonography is performed routinely for the evaluation of any suspicious mass located in the posterior segment, especially in the patients with media opacity. For the diagnosis of choroidal melanomas, this method helps to determine not only the correct diagnosis, but also to evaluate possible extraocular enlargement, to estimate the size of the tumor after periodic recurrent observations, and to appropriately schedule a therapeutic intervention.

Intraocular melanomas have several characteristics as follows:

- An acoustic quiet zone at the base of the tumor called acoustic hollowing.
- Low-to-medium reflectivity.
- Internal vascularity.
- Excavation of underlying uveal tissue.
- Shadowing of subjacent soft tissues.

Ultrasound biomicroscopy (UBM) uses high-frequency waves. This method has excellent resolution and is therefore suitable for the diagnosis of anterior ocular abnormalities. It has ability to distinguish very frontal choroidal melanomas from those that originate from the ciliary body. Moreover, it can help define the frontal plane of the tumor or help to assess angle closure glaucoma.

3.4.2. Angiography and radiography

In case of doubts, diagnostics of choroidal melanoma can be confirmed by fluorescein angiography or indocyanine green angiography, mostly in cases, when the lesions do not show

pathogenic symptoms. Fluorescein angiographic changes, which can be observed in small choroidal melanomas, may be similar to some choroidal nevi. Such changes range from normal angiography findings to hypofluorescence developed secondary to blockage of the background fluorescence. In larger melanomas, a patchy pattern of early hyper- and hypofluorescence may occur, which can be followed by late intense staining. In some cases, choroidal melanomas can develop their own internal vascularization so that appear on the angiogram. Simultaneous fluorescence of the choroidal and retinal circulation in the tumor is an angiographic feature, called the “double circulation model.” Its occurrence differs from choroidal melanomas.

3.4.3. *Computed tomography*

Computer tomography (CT) imaging method is more expensive and less sensitive compared to ultrasonography. However, it is used for scanning of the eye globe and orbit due to its ability to visualize extraocular tumor growth and to help distinguish between choroid or retinal detachment and solid tumor.

Prior to this examination, application of intravenous injection of the contrast agent is needed. As a result, contrast will cause enhancement of choroidal melanoma, whereas in case of exudation will not.

3.4.4. *Magnetic resonance imaging*

Magnetic resonance imaging (MRI), also used for scanning the eye globe and orbit, is even more expensive than CT scanning and less sensitive than ultrasound. However, MRI uses surface coil imaging and gadolinium as a contrast material for improving its resolution. Within the MRI, high-density lesions represent T1-stage pigmented melanomas, and low density can exhibit pigmented melanoma at T2 stage. In many cases, MRI is used to determine the extra-scleral melanoma enlargement or to distinguish surrounding fluid from the tumor.

3.4.5. *Biopsy and genetic analysis*

Practice usually does not require the use of a fine needle biopsy and an incisional biopsy. However, these additional examination methods may be useful in differential diagnosis. They are used to distinguish amelanotic melanomas from metastatic tumors and as complementary tests, if the results of other tests are ambiguous. It is possible to achieve more than 95% accuracy in tumors larger than 3 mm using both types of biopsy. Comparing both methods, incisional biopsy is more invasive and comes with higher complications rate, but has lower rate of falsely positive or negative results. Intralesional or perilesional hemorrhage are the most common complications, a fine needle biopsy is not connected with higher risk of spreading cancer cells in the case of choroidal melanoma.

Following biopsy, the prompt treatment is indicated with an aim to prevent extrascleral extension.

Nowadays, genetic analysis and karyotyping of biopsy samples are becoming more important. Various studies have documented that Chromosome 3 monosomy in the choroidal tumor is associated with a significantly higher risk of developing metastatic process. Nowadays, sadly, there is still no effective treatment for metastatic disease available.

3.5. Treatment opportunities

The important prognostic indicators they initiate the following therapy for posterior uveal melanoma are the age and the volume (size) of the tumor. Many studies are documenting that over 50% of patients with uveal melanoma die because of direct or indirect reasons (e.g., metastasis) within 15 years after the therapy, although radical surgery (enucleation) or other therapeutical methods are used.

In turn, modern diagnostic tools, they include ophthalmological examination, CT, and MRI brought most vital advances in the ability of primary uveal melanoma diagnosis. The diagnostic methods have radically improved in the last decades, and different types of radio surgery (external beam, charged particle or brachytherapy) have become the preferred treatment in significant number of patients with uveal melanoma. One of the main reasons for the development of alternative therapies is the objective of promoting survival and maintaining vision in patients who have experienced uveal melanoma. Among other things, many types of radiation are used in today's treatment of posterior uveal melanoma. One of the representatives of the "conservative" approach is stereotactic radiosurgery (SRS) with the usage of a linear accelerator.

In addition to SRS, the gamma-knife radiosurgery method is used. Both methods provide good local control with survival rates comparable to other treatments. SRS of extracerebral lesions, such as uveal melanoma, has been invented about 20 years ago. An alternative treatment that has been proven to treat middle and large posterior choroidal melanoma is the SRS method. Another method is the plaque radiotherapy, when the eye globe salvation is achieved. It is used especially in cases of tumor location outside the optical disc or the macula. The positive consequence for the patient is the useful vision that can be retained after treatment. Linear accelerator therapy with a single fraction of the intraocular tumor is considered to be a relatively unusual approach to the treatment of uveal melanoma. For treatment planning coordinates is used an image fusion of a contrast-enhanced MRI and CT. When using a collimation system in an operation, it is important to achieve spatial accuracy when administering one fraction [9–11].

4. Stereotactic radiosurgery for intraocular tumors

Stereotactic radiosurgery was initially developed in 1949 by Lars Leksell, the Swedish neurosurgeon, who treated small targets of tumors located in the brain. It was a new step in radiotherapy methods. Nowadays, the stereotactic radiosurgery (or external beam irradiation with protons or helium ions) is a regularly used option in the treatment of mainly medium-sized choroidal melanomas. In many cases, it has been applied for larger tumors. Eye globe and orbit scanning by CT or MRI is necessary for verifying of extraocular extension. It is necessary to use these techniques to differentiate between choroidal tumor and primary versus secondary retinal detachment. Every patient with a medium-sized melanoma is sent to chest X-ray, liver ultrasound, and general examination but also to PET/CT to detect possible metastases.

Methods like MRI, CT and also digital subtraction angiography (DSA) are included in imaging equipment. Structures of the eye globe and lesions are defined, visualized and localized.

Software for target verification, which is used in conjunction with stereotactic frame system and imaging (CT, MRI) modalities, is used to determine the coordinates of the lesion (tumor) target into the stereotactic frame reference system.

The radiosurgical treatment is calculated by physicist by planning system for treatment (TPS) with the 3-D dose distribution. The result is superimposed onto the certain patient's anatomical status to get an appropriate radiation dose for tumor and also for risk structures (optic nerve, lens, chiasm, etc.) and radiosurgical procedure [12–14].

5. 3D printed models of the intraocular melanoma for planning of stereotactic radiosurgery treatment

Stereotactic radiosurgery (SRS) is a technically challenging therapeutic irradiating method. It complements or supplies (replaces) classic surgical intervention. It is used for single high-therapeutic irradiation dosage to an exact specified volume, while risk organs and structures are contemporary protected. A prerequisite for this method is a special software and hardware equipment of workstation and professional experiences of specialists of different fields (neurosurgeon trained in stereotactic radiosurgery, radiation oncologist, ophthalmologist, radiologist, clinical physicist and registered nurse trained for radiosurgery).

The surgical operation involves the selection and preparation of the patient prior to surgery intervention, which consists from processing of health and imaging documentation of the patient. It is necessary to analyze the patient's disease and the patient's indication by the Indicating Commission (BTB). The Commission decides about the indication in which the members are neurosurgeons trained in radiosurgery, radiation oncologists, ophthalmologists, radiologists and clinical physicists. The progress committee decides on the basis of a recommendation on the appropriateness of an eye globe oncological surgery, the listed group of experts will evaluate the suitability of classical surgery, stereotactic radiosurgery operations, fractionated stereotactic radiosurgery, intensity modulated radiotherapy (IMRT) or three-dimensional comfort radiotherapy (3D-CRT).

Patients indicated for stereotactic radiosurgical intervention are hospitalized for inpatient care. This is a short-term hospitalization, most often lasts 3 days. The patient admission involves interview with the patient with detailed information about the course of operation, performance benefits as well as acquaintance with potential acute and late postoperative complications (adverse effects). The patient subscribes the informed consent.

Patient's admission in hospital bed department (clinical care) is carried out 2 days before the surgery. A detailed clinical examination will be done, brought documentation is studied, the missing examinations are completed and a preoperative pharmacotherapy treatment in hospital bed department is placed on. Findings, surgery and documentation will be inserted into the hospital information system. The day before the stereotactic radiosurgery (SRS) will be initiated the patient's pharmacotherapy—premedication. Within the preoperative premedication, the patient is receiving the antiedematotic therapy, which intensity depends on the size, location of the lesion and the presence of edema. The presented therapy is continued in the day of surgery and the following day.

Each patient's record includes the tumor size, tumor volume, the maximum height of the tumor, age and gender, the presence and the extent of secondary retinal detachment, and the possible signs of extrascleral extension. The very important step of SRS is tumor volume calculation in each patient directly by results of CT and MRI examination. It is the basic step involved to the stereotactic planning scheme.

Immobilization of the affected eye globe for stereotactic irradiation is achieved by mechanical fixation of the sutures to the Leibinger stereotactic frame. Vicryl sutures from four extraocular muscles (m. rect. sup., m. rect. inf, m. medialis and m. temp.) are placed through the conjunctiva and the lids. The stereotactic frame is fixed to the head, and the sutures are tied to the stereotactic frame. The day after stereotactic irradiation is the patient examined by an ophthalmologist (the slit lamp examination, ophthalmoscopy, and intraocular pressure measuring) and is released for home treatment, he gets antibiotic and corticosteroid eye drops.

In software for data segmentation (3D Slicer, freeware version 4.5.0+), virtual 3D models of the eye globe were created. Imported data set came from CT (computer tomography) with accuracy 1 mm scan thickness. Visualized and created model has basic anatomical structures like globe, corneal segment, lens, optic nerve and tumor mass inside the created 3D model of eye globe. Extraocular muscles and vitreous body are not included in the model. Eye globe anatomical structures—lens and optic nerve—are very important for orientation. They are necessary visible points at the small printed 3D model because the model itself has the same size as the normal human eye globe—from anterior to posterior part is 24 mm. Virtual 3D model of the eye globe is then sliced. Additional support is calculated. The next step can be model preparing for printing in 3D printing slicing software Simplify3D. After creating and refining our models, for process of 3D printing, we used fused deposition modeling (FDM) technology. The 3D models in our study are printed on ZYYX 3D Printer by Magicfirm LLC using one extruder heated to 215–230°C. Chosen material is polylactic acid (PLA) with low deformability during rapid temperature changes and contributing high accuracy of the model. One layer of the model thickness of in vertical line is 100 µm. This provided an ideal proportion of a ratio between accuracy and velocity of a printing process. Estimated time of printing process in 3D printer is usually from 15 to 30 min per one model (**Figures 2 and 3**).

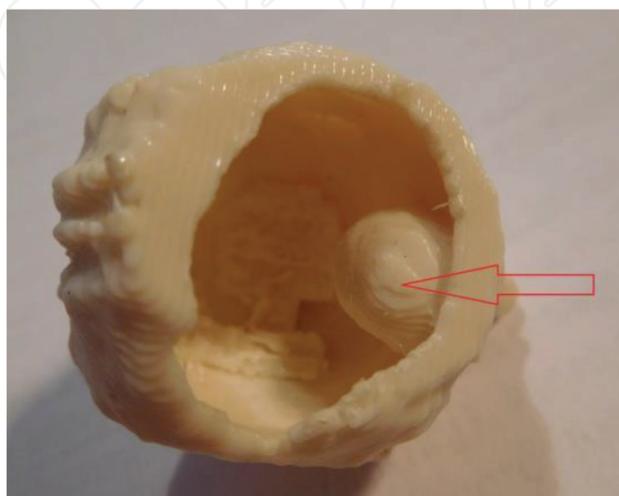


Figure 2. 3D printed model of the eye globe with intraocular tumor—arrow shows the tumor mass (melanoma).

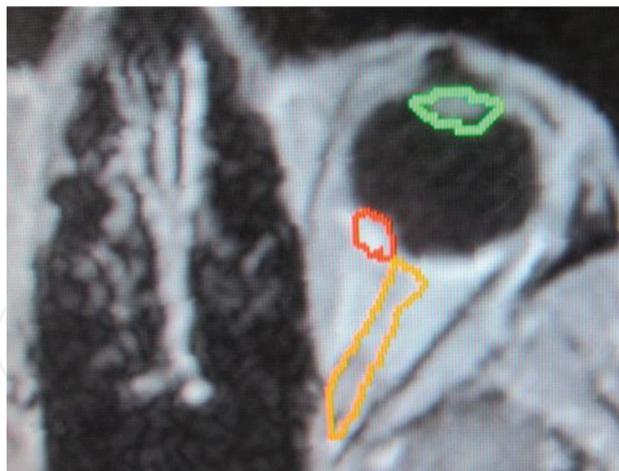


Figure 3. MRI scan of eye globe with uveal melanoma (choroidal melanoma stage T1b)—red color, lens—green color, optic nerve—yellow color.

Stereotactic one-day session therapy of intraocular uveal melanoma, based on CT and MRI images, is a precise treatment option and safe. The results of the treatment were summarized in the study and demonstrated that the local control was excellent. Among other results, they have further shown that in patients with an unfavorable tumor size and localization near critical structures such as the optic nerve, lens and macula, visual acuity has been reduced. In the patient's follow-up after 6 months, visual acuity was evaluated. The study included a group of 77 patients in whom 85.5% of patients had a visual acuity of 0.1 or higher before radiotherapy. In the cases with intraocular uveal melanoma, these patients may be recommended to undergo LINAC-based one-day session stereotactic irradiation, especially in the cases of medium-sized uveal melanomas. Important advantage of this treatment method is preserving of the eye globe [5, 6].

6. Discussion

In the treatment of the uveal melanoma patients, stereotactic irradiation has been used over 20 years. Over time, the therapeutic single dose decreased and stabilized at 35.0 Gy. In the studies, this reduction did not lead to tumor control reduction. The studies also documented that hypofractionated treatment is beneficial. This treatment uses a very large fraction to stabilize the intraocular uveal melanoma cell lines.

In the last years, additional interest in fractionated stereotactic radiotherapy (SRT) was obtained. Feasible fractionation advantage is used by Linear accelerators (LINAC). Nowadays, therapeutic schemes for hypofractionated therapy for five fractions with total doses from 50.0 to 70.0 Gy are employed by most LINAC studies. Different studies report local tumor with control rates more than 90% by the efficacy of SRT in uveal melanoma treatment. In treatment

of melanoma close to the optic disc, juxtapapillary choroidal melanoma, this stereotactic radiotherapy offers another non-invasive alternative to radical surgery—enucleation—or to brachytherapy treatment with high tumor control rate [9, 15].

The gamma knife radiosurgery and SRS are evaluated as the alternative in patients with large tumors (stage T3) which are too large for conventional brachytherapy. Studies confirm with their results that treatment with SRS may also be recommended in specific cases of uveal melanoma [16, 17].

Interesting is the comparison with other forms of radiotherapy. Typical side effects of radiation from SRT include: radiation retinopathy, cataract development, secondary neovascular glaucoma, and opticopathy. The result may be loss of visual acuity. In the worst cases, secondary enucleation is necessary. However, even with these risks, SRS and SRT are among the most effective treatments for uveal melanoma. The SRS method belongs to one of the new methods; therefore, it is needed to record and compare results with other methods by a multicenter studies. Treatment of uveal melanoma using a combination of stereotactic photon therapy and CT and MRI scans is considered very safe and accurate and guarantees excellent local control. A reduction in visual acuity was observed in a large number of patients. This condition was a result of the unfavorable size and position of the tumor near critical structures, such as the optic nerve and the macula. Obtained patient observations confirmed that stereotactic irradiation for uveal melanoma using LINAC is feasible and well tolerated. This treatment preserves the patient's eye globe and is offered in the case of moderate or unfavorably localized uveal melanomas [5].

Optical neuropathy may rarely occur after radiosurgical treatment of lesions that are located near visual pathways. A highly effective method in these cases for the treatment of small and moderate uveal melanomas is a one-step LINAC-based SRS with a single dose of 35.0 Gy. This treatment involves the use of a mechanical immobilization system with four stitches [18].

3D printing has gained its new role in ophthalmology by confirming and demonstrating the real shape and size of tumors by creation of accurate 3D models. With current advances of precise modeling process, material to build the 3D models can be printed at 600 μm resolution. This approach is already in use within the other fields of ophthalmological surgery. An example is the use in cataract surgery—development of Cana's Ring (CR) and a special expansion device for 3D pupils [19].

Another example of the practical use of 3D printing in ophthalmology is the eye fundus examination. The correct collocation of the patient, the smartphone and the Volk spherical lens is extremely important. To secure the correct position, a 3D printed adapter from plastic was created to connect the lens with the smartphone together [20].

Different studies evaluated the efficacy of stereotactic radiosurgery as a treatment modality for uveal melanoma. Tumor control rates 5 and 10 years after therapy were over 90% in several studies. Results of these studies did not show a significant difference between radiogenic side

effects of SRS and other forms of radiotherapy. Majority of visual acuity decline and necessity of secondary enucleation are neovascular glaucoma. Radiation therapy of stereotactic photon beams for the treatment of intraocular melanoma is considered effective nowadays. However, it is still recommended for future studies and follow-up actions to focus on finding optimal treatment modalities [21].

3D printed model of eye globe with tumorous mass is due to our experience helpful during the stereotactic planning process. Planning of stereotactic radiosurgery is based on fusion of CT and MRI data. Understanding of the collocation of all the structures of the eye globe with critical structures inside, such as lens, optic disc and the tumor size and its location, is a basic condition for the planning software.

By introducing a new 3D modality for visualization of the eye globe with the tumor, we provided real model of the eye globe for the specialists, which enabled them increase effectiveness of the planning process during the stereotactic radiosurgery. Virtual 3D model can be seen on computer only, but real printed 3D model of the eye globe held by the physician and physicist in their hands gives them a better perspective of the real situation inside the eye globe, like the size, the distance of the tumor to critical structures, the lens, optic disc and optic nerve [5].

7. Conclusions

The number of patients in our study with reduced visual acuity will probably increase in the future. Created model was used for comparison with pictures of the eye globe after enucleation due to secondary complications (amotio retinae). In future, we plan to make a collection of interesting models of rare cases for purposes of education.

Current possibilities of creating the real-sized or even also enlarged 3D models of the affected eye globe help ophthalmologists and other specialists to comprehend and visualize the size and localization of the tumor, has been rather difficult before, solely with the 2D radiographic imaging. The 3D model of an eye globe with an intraocular tumor has an important role during the process of preparing a stereotactic radiosurgery planning scheme. This is a step forward for the team of specialists responsible for management and treatment of a patient with malignant melanoma. Implementation of a 3D model in the process of individualized irradiation planning of stereotactic surgery has a great potential for the future.

Conflict of interest

None of the authors has conflict of interest with this submission.

Author details

Alena Furdova^{1*}, Adriana Furdova¹, Miron Sramka², Robert Furda³ and Gabriel Kralik⁴

*Address all correspondence to: alikaufurdova@gmail.com

1 Department of Ophthalmology, Faculty of Medicine, Comenius University, Bratislava, Slovakia

2 Department of Stereotactic Radiosurgery, St. Elisabeth Cancer Institute, St. Elisabeth University College of Health and Social Work, Bratislava, Slovakia

3 Department of Information Systems, Faculty of Management, Comenius University, Bratislava, Slovakia

4 Department of Medical Physics, Faculty of Medicine, Slovak Medical University, Bratislava, Slovakia

References

- [1] Ventola CL. Medical applications for 3d printing: Current and projected uses. *Pharmacology & Therapeutics*. Oct 2014;**39**(10):704-711
- [2] Prasad TS, Sujatha G, Muruganandhan J, Patil S, Raj AT. Three-dimensional printing in reconstructive oral and maxillofacial surgery. *The Journal of Contemporary Dental Practice*. Jan 1, 2018;**19**(1):1-2
- [3] Valverde I, Gomez G, Suarez-Mejias C, Hosseinpour A-R, Hazekamp M, Roest A, et al. 3D printed cardiovascular models for surgical planning in complex congenital heart diseases. *Journal of Cardiovascular Magnetic Resonance*. Feb 3, 2015;**17**(Suppl 1):P196. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4328535/> [Accessed: Apr 14, 2018]
- [4] Huang W, Zhang X. 3D printing: Print the future of ophthalmology. *Investigative Ophthalmology & Visual Science*. Aug 1, 2014;**55**(8):5380-5381
- [5] Furdová A, Sramka M, Thurzo A, Furdová A. Early experiences of planning stereotactic radiosurgery using 3D printed models of eyes with uveal melanomas. *Clinical Ophthalmology (Auckland, N.Z.)*. Jan 31, 2017;**11**:267-271
- [6] Furdová A, Furdová A, Thurzo A, Šramka M, Chorvát M, Králik G. Possibility of 3D printing in ophthalmology—first experiences by stereotactic radiosurgery planning scheme of intraocular tumor. *Ceská a Slovenská Oftalmologie*. Fall 2016;**72**(3):80-84
- [7] Shields JA, Shields CL. *Intraocular Tumors: An Atlas and Textbook*. Philadelphia, Pa.: Lippincott Williams & Wilkins; 2008. 598 p

- [8] Furdova A, Sramka M. Uveal Malignant Melanoma and Stereotactic Radiosurgery: Intraocular Uveal Melanoma and one-Day Session Stereotactic Radiosurgery at Linear Accelerator. Saarbrücken: LAP LAMBERT Academic Publishing; 2014. 188 p
- [9] Mueller AJ, Talies S, Schaller UC, Horstmann G, Wowra B, Kampik A. Stereotactic radiosurgery of large uveal melanomas with the gamma-knife. *Ophthalmology*. Jul 2000; **107**(7):1381-1387 (discussion 1387-1388)
- [10] Tokuuye K, Akine Y, Sumi M, Kagami Y, Ikeda H, Kaneko A. Fractionated stereotactic radiotherapy for choroidal melanoma. *Journal of the European Society for Radiotherapy and Oncology*. Apr 1997;**43**(1):87-91
- [11] Furdova A, Strmen P, Waczulikova I, Chorvath M, Sramka M, Slezak P. One-day session LINAC-based stereotactic radiosurgery of posterior uveal melanoma. *European Journal of Ophthalmology*. 2012;**22**(2):226-235
- [12] Zehetmayer M, Kitz K, Menapace R, Ertl A, Heinzl H, Ruhswurm I, et al. Local tumor control and morbidity after one to three fractions of stereotactic external beam irradiation for uveal melanoma. *Journal of the European Society for Radiotherapy and Oncology*. May 2000;**55**(2):135-144
- [13] Hungerford JL. Current trends in the treatment of ocular melanoma by radiotherapy. *Clinical & Experimental Ophthalmology*. Feb 2003;**31**(1):8-13
- [14] Selby BP, Sakas G, Walter S, Groch W-D, Stilla U. Pose estimation of eyes for particle beam treatment of tumors. In: *Bildverarbeitung für die Medizin 2007* [Internet]. Berlin, Heidelberg: Springer; 2007. pp. 368-373. (Informatik aktuell). Available from: https://link.springer.com/chapter/10.1007/978-3-540-71091-2_74 [Accessed: Apr 14, 2018]
- [15] Krema H, Somani S, Sahgal A, Xu W, Heydarian M, Payne D, et al. Stereotactic radiotherapy for treatment of juxtapapillary choroidal melanoma: 3-year follow-up. *The British Journal of Ophthalmology*. Sep 2009;**93**(9):1172-1176
- [16] Dieckmann K, Georg D, Zehetmayer M, Bogner J, Georgopoulos M, Pötter R. LINAC based stereotactic radiotherapy of uveal melanoma: 4 years clinical experience. *Radiotherapy and Oncology*. May 2003;**67**(2):199-206
- [17] Furdova A, Sramka M, Chorvath M, Kralik G, Krasnik V, Krcova I, et al. Stereotactic radiosurgery in intraocular malignant melanoma--retrospective study. *Neuro Endocrinology Letters*. 2014;**35**(1):28-36
- [18] Furdova A, Sramka M, Chorvath M, Kralik G. Linear accelerator stereotactic radiosurgery in intraocular malignant melanoma. *Austin Journal of Radiation Oncology and Cancer*. 2015;**1**(2):1009
- [19] Canabrava S, Diniz-Filho A, Schor P, Fagundes DF, Lopes A, Batista WD. Production of an intraocular device using 3D printing: An innovative technology for ophthalmology. *Arquivos Brasileiros de Oftalmologia*. 2015 Dec;**78**(6):393-394

- [20] Myung D, Jais A, He L, Blumenkranz MS, Chang RT. 3D printed smartphone indirect lens adapter for rapid, high quality retinal imaging. *Journal of Mobile Technology in Medicine*. 2014;3(1):9-15
- [21] Zehetmayer M. Stereotactic photon beam irradiation of uveal melanoma. *Developments in Ophthalmology*. 2012;49:58-65

IntechOpen

IntechOpen

