POSSIBILITY OF 3D PRINTING IN OPHTHALMOLOGY – FIRST EXPERIENCES BY STEREOTACTIC RADIOSURGERY PLANNING SCHEME OF INTRAOCULAR TUMOUR

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SUMMARY

POSSIBILITY OF 3D PRINTING IN OPHTHALMOLOGY – FIRST EXPERIENCES BY STEREOTACTIC RADIOSURGERY PLANNING SCHEME OF INTRAOCULAR TUMOR

Nowadays 3D printing allows us to create physical objects on the basis of digital data. Thanks to its rapid development the use enormously increased in medicine too. Its creations facilitate surgical planning processes, education and research in context of organ transplantation, individualization prostheses, breast forms, and others.
Our article describes the wide range of applied 3D printing technology possibilities in ophthalmology. It is focusing on innovative implementation of eye tumors treatment planning in stereotactic radiosurgery irradiation.
We analyze our first experience with 3D printing model of the eye in intraocular tumor planning stereotactic radiosurgery.

Key words: 3D printing, model, Fused Deposition Modelling, stereotactic radiosurgery, prostheses, intraocular tumor

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At present 3D printing, thanks to its extremely rapid advance, is enabling the creation of models of objects, structures and shapes which would have appeared impossible a few years ago. Currently two dozen methods of 3D printing are known, which differ in the technology of the printer itself, the printing speed, resolution, printed material etc. These technologies are capable of creating models on the basis of templates of practically any shape, virtually modelled as computer-aided design (CAD) files. In the basic configuration the 3D printer follows the instruction of the CAD file for creating a basis for an object moving on the x-y level. Subsequently the printer proceeds by moving vertically in the z axis in order to create layers of the object one upon another. It is important to know that the outputs of 2D imaging methods such as RTG, magnetic resonance (MRI) or computer tomography (CT) can be transformed into 3D files with individualised imaging of anatomical structures. Through the process of applying material – e.g. plastic, ceramics, metal or even live cells – one layer upon another, the printer progressively creates a three-dimensional object with high precision according to a virtual model.

Methods of 3D printing have been used for several years, primarily for the creation of product prototypes. Several plants use large 3D “rapid prototype machines” for creating models and forms. In medicine 3D printing has been applied since the beginning of this millennium, when it was used for creating dental implants and individualised prostheses. Since then it has developed rapidly and its use has spread into several branches (4, 6).

History of 3D printing: In the 1980s Charles Hull invented 3D printing, also known as “stereolithography”. Stereolithography uses the format .stl for interpretation of data in a CAD file, by which it enables these instructions to be formulated electronically for a 3D printer. Together with information about shapes, .stl may incorporate data about colour, texture and thickness of the printed object. Hull later founded the company 3D Systems, which created the first 3D printer, also known as “stereolithography apparatus”. In 1988 the company began to manufacture the first commercially available printer SLA-250.

Most widespread methods of 3D printing: All the processes of three-dimensional printing present both advantages and disadvantages. The selection depends on the material we wish to use and the method by which we want the individual layers to be applied in the resulting object. The three most widely used technologies of 3D printing in the field of medicine are selective laser sintering (SLS), thermal inkjet (TIJ) and fused deposition modelling (FDM).

Selective Laser Sintering uses powder materials for printing new objects with high precision. The laser sketches the shape of the object in powder, by which it causes its fusion. Subsequently a new layer of powder is applied and the process is repeated layer upon layer until the formation of the entire model. This method is used especially in printing from ceramics, plastic and metal.

Thermal Inkjet Printing is a "contact-free" method, which uses thermal, electromagnetic or piezoelectric technology for applying small drops of atramentum (or other material) into a substrate according to digital instructions. The location of the drop is usually fixed with the use of heat or mechanical compression. By heating the printhead small air bubbles are formed, which upon bursting cause a print wave forcing the drop of atramentum from the jet in the a volume of 10-150 picolitres. The use of these printers sounds promising within the framework of the field of regenerative medicine and "bioprinting", thanks to its digital precision and benign effect on live cells.

Fused deposition modelling is a far more widely used and cheaper method than SLS. An FDM printer uses a head similar to an inkjet printer, but instead of atramentum releases heated plastic material during its movement from the jet (extruder), by which it builds and object thin layer upon layer. As the material hardens, the individual layers bond together and obtain their firmness. Depending on the complexity and price of the FDM printer it is possible to print with the help of various plastic materials and several extruders at once (9, 10).

Present use of 3D printing in ophthalmo(onco)logy: Use also within the framework of ophthalmology is of exceptionally high interest. It incorporates application in the field of the optics industry and printing of glasses to bioprinting of tissues, such as the sclera and cornea (4). Form prostheses and epitheses for patients for patients following mutilating procedures with an ocular tumour are produced far cheaper and faster with the aid of a 3D printer, in comparison with classically manually produced forms which take up to several weeks (8). Following traumatic injuries to the eye socket with its subsequent reconstruction, individualised forms are used for creating a titanium implant before surgery is performed on the patient. This substantially reduces the time of the procedure, in which it is not essential to inspect and adapt the implant in the open bone defect perioperatively. On the basis of imaging methods everything is conveniently prepared before the beginning of the operation, and the surgeon thus has a greater overview of the complexity of the fractures. Models subsequently serve for explanation for the patient or for educational purposes within the framework of further education, not only for professionals but also for students. Screening of ocular pathologies is made easier by created 3D inventions enabling convenient visualisation of the ocular fundus with the aid of a smart phone in developing countries as a practical substitute for an expensive and physically cumbersome fundus camera (6). The latest method of use of a 3D printer in the field of ophthalmic oncology is the creation of a real model of the eyeball with an intraocular tumour for the process of sketching and planning the procedure of stereotactic radiosurgery.

Stereotactic radiosurgery: The planning of a stereotactic operation is based on imaging obtained with the aid of CT and MRI. At some clinical workplaces other imaging methods are preferred – PET, angiography, MR spectroscopy etc. The obtained images serve for precise determination of the anatomical structures – differentiation of target volume, tumour from healthy tissue, mainly critical structures and determination of their stereotactic co-ordinates to which radiation beams are to be applied (1, 2). Upon planning the smallest possible depth of incision is always chosen – most frequently 1 mm with regard to the small anatomical dimensions of the eye. After imaging on CT and MRI the individual sets of incisions are transferred by computer into the planning system. Before the actual planning of radiation treatment, fusion of the CT and MRI images is performed.

CT imaging is important for determining the boundaries of the target volume, the imaging takes place on the basis of a different electron density caused by the different atom structure of the tissues. In addition to anatomical imaging, after mathematical conversion CT imaging provides precise values of electron density in the forms of electrons in 1 pixel. This information in the form of a map is used upon definition of the isodose lines in the planning system. Without information about electron density the planned isodose distribution could differ by up to 20% as against the actual distribution of the dose, due to the influence of neglect of the heterogeneity of the tissue. Even upon the use of contrast substances, above all intracranially, CT imaging of soft tissues is not optimal. MRI is also used as a further imaging modality, providing an image on the basis of an analysis of different absorbed and emitted energies following the excitation of hydrogen nuclear spins of water and fats, which were excited and directed in the magnetic field. Through a combination of information obtained from the images it is possible to attain a better definition of the edges and total volume of the target structure. Upon planning the smallest possible depth of incision is always chosen – most frequently 1 mm with regard to the small anatomical dimensions of the eye. After display on CT and MRI the individual sets of incisions are transferred by computer into the planning system. Before the actual planning of radiation treatment, fusion of the CT and MRI images is performed (3, 5).

Fusion of the images is processed with the aid of mathematical software, which fuses the created volumes of the head generated on the basis of CT and MRI images. Sketching of the structures takes place with the aid of MRI images, but is performed into the supporting CT images. This may be performed either manually or automatically. In radiation treatment highly radiosensitive neuroanatomic structures are considered to represent risk structures. In the case of radiation of intraocular tumours, both lenses are sketched into the plan, as well as both optic nerves, the chiasma opticum, brain stem and skin of the head. Sketching of the skin or surface is important upon calculation of the penetration depth for each beam during calculation of the dose (7). It is precisely the subjectivity of manual sketching by an expert, influenced with the aid of a printed 3D model, that is able to assist visualisation within real space substantially, and thus increase the precision of sketching of the target structure.

Planning of distribution of dose into target volume: The individual measures in planning are influenced by several configurations and the used planning system. The aim of planning is to locate the optimum setting of the number and locality of the isocentres, the size and type of used reflector sights and the weight of the individual oscillations in order to ensure that the resulting radiation corresponds with the condition of radiation of the tumour deposit with a therapeutic dose and minimises damage to the surrounding structures. The selection of radiation beam directions is mediated with the aid of tools such as a beam's-eye-view (BEV) or visualisation of digitally reconstructed radiographs (DRR).

According to the scheme of planning and the possibilities for setting the parameters we differentiate between direct and inverse planning. Direct planning works on the principle of proposed parameters (size of reflector sights, angle of oscillation, number of oscillations etc.), which can be appropriately modified during planning up to a point where according to the operator it is not possible to improve the plan with regard to the given conditions. In inverse planning the limit doses are determined in the defined volumes, as well as the basic setting of the number and angles of oscillations. The optimisation system then determines the best possible configuration of radiation parameters on the basis of the entered values. These may then be further adjusted according to requirement by the operator.

In direct planning of radiation treatment it is possible in general to influence the distribution of the dose by three methods: balancing of the curve, alteration of curve range and application of several isocentres. The basic configuration originates from the University of Florida. Distribution of the dose ensues from 9 evenly distributed non-coplanar curves with a range of 100°. The result is a spherically distributed dose, which decreases evenly in each direction. The method presupposes the use of tube reflector sights.

The plan can be adjusted further by balancing the curves and altering their range, this planning scheme is entitled the technique of multiple non-coplanar curves. The aim of further configurations is to alter the distribution of the dose from spherical to ellipsoid, or to a shape which best describes the target volume. By reduction of the mass of the curve to zero it is possible to achieve a fundamental alteration of radiation of the spherical volume to ellipsoid. In the case of ellipsoid volume oriented laterally, the mass of 3 central / vertical curves is reduced. If the ellipsoid volume is oriented sagittally, the 2 lateral curves are reduced from both sides. In general curves are eliminated which are the most perpendicular to the extended axis of target volume of ellipsoid shape. With the elimination of certain curves the gradient of the dose is increased, and thereby also the conformity of the given plan. Further adaptation of the distribution of the dose is possible by altering the mass of certain curves and replacing the reflector sight with a larger or smaller diameter. This results in further sparing of the surrounding structures and an increase of the conformity of the plan. In addition to the mass of the curve, its range can also be altered, i.e. the angle between the starting and end position of the gantry. The range of the curve is altered from the base setting in the case that the target volume is in a certain incline with a horizontal plane. The range of the curve is then shortened so that its axis overlaps with the main axis of target volume. The result of constriction of the curve range also leads to an alteration of the distribution of isodoses, which are extended in the direction of the axis of the angle.

The method of multiple isocentres is used most often in the case of irregular shape of the target volume. In general if the volume is of cylindrical shape, 2 isocentres are proposed. If it is of a pyramid shape, 3 isocentres are used. If it is of a quadratic shape, 4 isocentres are used. In the case of specific requirement a larger number of isocentres may be proposed. Following computer reconstruction of the target volume, its plane is determined, which contains the main axis. For the selected number of isocentres, mass and range of the curves, the created plan is optimised further according to requirement. Dynamic stereotactic radiosurgery presupposes mutual movement of the gantry and radiation table. The patient, lying on his/her back is affixed to the radiation table in the place of the stereotactic frame. The gantry rotates in a total angle of 300° (interval 30°-300°) and the table at an angle of 150°(interval -75°- 75°), movement is synchronised so that 2° of rotation of the gantry corresponds to 1° of rotation of the table. Several techniques for calculating the dose exist for SRCH planning. SRCH systems on a linear accelerator with tube reflector sights use calculation of the dose on the basis of the TMR (tissue-maximum ratio) values and dose profiles, which are a function of the depth and can be measured. For each oscillation the average TMR is calculated for all beam directions that contributed to the dose of the oscillation. The total distribution of the curve is approximately calculated on the basis of approximation of the continuous oscillation to a series of individual beams.

Planning systems differ also in their allowance for the heterogeneity of the tissue upon calculating the distribution of the dose. In general, upon intracranial radiation brain tissue is considered homogeneous and the procedure neglects to differentiate bones, brain tissue and cavities filled with air mainly with regard to the simple geometry. It is assumed that the value of maximum error in TMR upon neglect of heterogeneity caused by the skull is approximately 1% for a beam with energy of MeV. At present the latest systems upon distribution of the dose correct the calculation with regard to the heterogeneity of the environment. An example of a direct planning system is STP 3.40-2 (Leibinger GmbH, Germany), which is used in radiation treatment with tube reflector sights. Inverse planning uses for example the

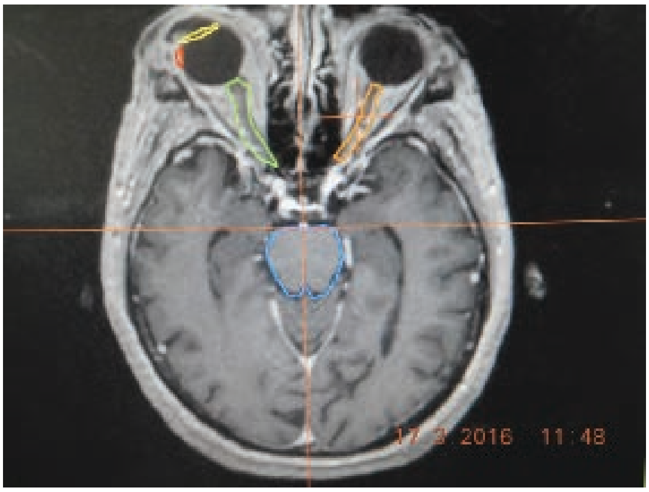

Fig. 1 Measuring MRI examination of patient before stereotaxis with sketching of the tumour deposit (red colour) and risk structures – lenses (yellow), optic nerve (green and orange) and brain stem (blue)

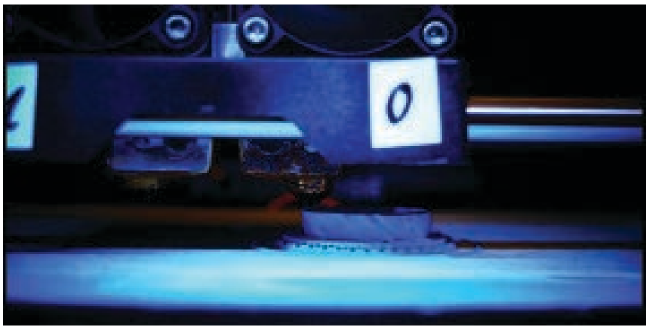

Fig. 2 3D detail of printhead during printing of model of eye with intraocular tumour

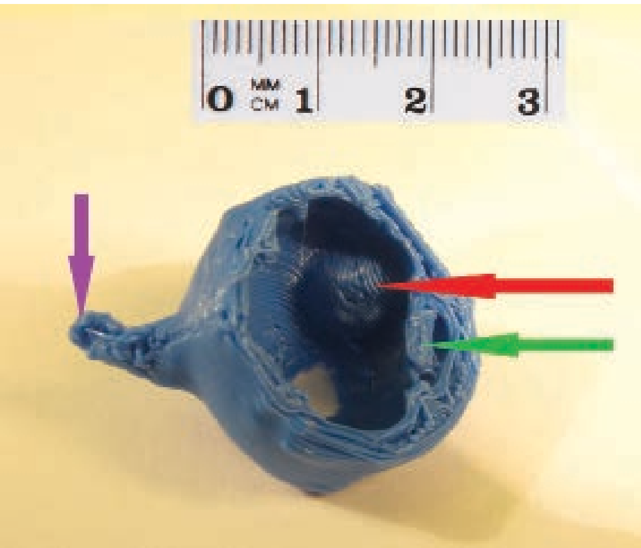

Fig. 3 Final 3D model of eye with intraocular tumour – tumour deposit (red arrow), lens (green arrow), optic nerve (purple arrow)

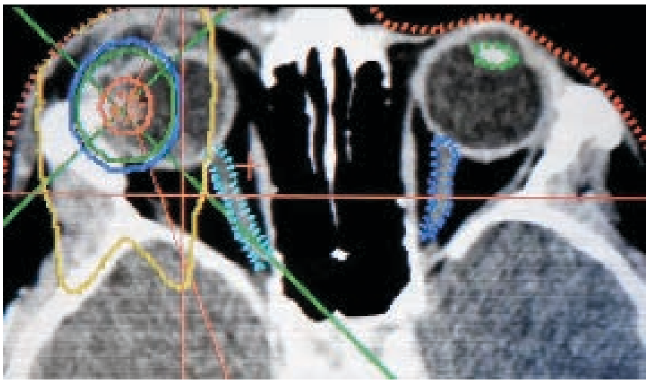

Fig. 4 Stereotactic radiosurgical plan of radiation treatment of patient with intraocular tumour – isodose distribution, tumour deposit indicated in red colour

system CORVUS 6.2 (CORVUS®, NOMUS Corporation, USA), which functions on the basis of IMSRCH with the aid of a multi-lamellar reflector sight with the commercial designation MIMiC. Both systems are currently used in planning and at the St. Elizabeth Oncological Institute (1, 2).

Use of 3D printing during planning of a stereotactic radiosurgical procedure: Through the use of software for segmenting data we created a 3D model of the wall of the eye with a growing mass of tumour, and also with visible anatomical structures of the internal wall, and if applicable the outgoing ocular nerve, the arrangement of which is exceptional for orientation within the framework of the model. For 3D printing we used the technology of fused deposition modelling (FDM), as material we selected polylactic acid (PLA), the properties of which guarantee low deformation of the model upon the sharp change of temperature during the process of 3D printing and thereby contribute to the precision of the physical 3D model. Retrospectively created prototype models serve for verifying the precision and comparing the size of the model with the tumour following enucleation on the basis of photography. We subsequently made use of these experiences upon compiling the specific stereotactic plan for patients. On the basis of the input data we were capable of creating a virtual model of the eye of patients with an intraocular tumour. Tumours indicated for stereotactic radiosurgery reach dimensions from 3 to 9 mm, and are frequently of bizarre shapes, which is difficult to imagine in an environment only with the aid of two-dimensional data from CT and MRI.

DISCUSSION AND CONCLUSION

Each year in Slovakia 20-30 patients are indicated for a stereotactic radiosurgical procedure due to a malignant intraocular tumour. It is precisely an understanding of the spatial layout and shape of the intraocular tumour in a materialised 3D model that substantially helps in targeted sketching of the given deposit in individual cross-sections of the image during the creation of the individual stereotactic plan for each patient. With the aid of 3D printing, models are now created as standard in medicine at centres of other disciplines (stomatosurgery, cardiosurgery, orthopaedics etc.), or as a diagnostic or therapeutic object with a marked contribution to the process of management of the patient's treatment (6, 7).

According to the data available to us, this technique has not yet been used to date in the field of ophthalmic oncology for the purpose of planning an actual stereotactic procedure. A further contribution in the case of progression of the pathology is the ability to assess the size of the tumour retrospectively following enucleation by comparison with the printed 3D model from the period shortly before the therapeutic procedure. Precisely due to the small dimensions of the eye as an organ, and therefore also the small dimensions of the tumour, we consider the introduction of a standardised, several times enlargement of the model.

When planning a stereotactic radiosurgical procedure the precision of sketching of the target tumour deposit and bordering of the risk structures is of decisive importance. We succeeded for the first time in materialising its shape and bordering using 3D printing and thus increasing the exactness of measurement of the therapeutic dose during individual planning of the procedure for patients, and by this method influencing the calculation of the lowest possible dose into the risk structures, which in many cases can determine the patient's quality of life after the procedure. In future we are planning to extend and create a set of models of the eye with different shapes of intraocular tumours, the contribution of which will be considerable also within the framework of the postgraduate treatment of doctors and students of medicine. The possibility of touching and seeing a 3D structure of the eye with a tumorous intraocular process is highly beneficial for the entire team that compiles the specific radiosurgical plan (clinical physician, stereotactic radiosurgeon, ophthalmologist), and contributes to a better understanding of the localisation and progression of intraocular tumours in comparison with the creation of a conception of the spatial layout exclusively with the aid of 2D imaging.

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