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Stereotactic Iodine-125 Brachytherapy for Low-Grade Glioma Treatment: A Monte Carlo study

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Abstract
Background: Stereotactic brachytherapy is an appropriate method that has been used for brain tumors and metastases treatment for more than 40 years for many patients in the world. Also, iodine-125 brachytherapy has been utilized in brain tumors for interstitial brachytherapy treatment since 1979. Even though the physical and biological features make these implants particularly attractive for minimal invasive treatment, the main goal of this paper is to evaluate the I-125 seed time and dose reached to brain glioma tumors of different sizes for treatment using Monte Carlo modeling.
Methods: In this paper, Monte Carlo simulation has been applied by the Gate code with 20 (MBq) activity for an iodine seed design for low-grade glioma tumors treatment. Dosimetry features of this source were defined by the updated TG-43U1 recommendations. The absorbed dose distribution around the seed was calculated using the Gate code in liquid water.
Result: The ideal condition for brachytherapy is for tumors smaller than 4 cm. With a larger tumor size, the absorption dose at the border of tumor and healthy tissue will be decreased and the implantation time for seeds will increase.
Conclusion: Placing an iodine-125 source inside the tumor is not sufficient because of the non-uniform dose distribution in the tumor and the length of treatment time. Using four iodine-125 sources eliminates the tumor, and also, a uniform dose distribution is created in the tumor and the implantation time will be reduced, respectively.
Keywords: Brachytherapy; Tumor; Iodine-125; Gate code simulation.

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Introduction

A brain tumor is the growth of an abnormal cell in the brain that may be benign (noncancerous) or malignant (cancerous). In other words, a tumor is a type of hard, hollow intracranial neoplasm, or an abnormal cell growth inside the brain or central spinal canal. Primary brain tumors are named according to the type of cells or the part of the brain where they begin to grow. For example, most primary brain tumors start in glial cells called glioma tumors. In adults, the most common types of brain tumors are gliomas and meningiomas.[1,2]

Glial cell functions are divided into four categories including: supporting the structure of the central nervous system, providing nutrition to the central nervous system, cleaning cellular waste, breaking down dead neurons. In general, three types of tumors grow from glial cells, including first and second-degree astrocytoma (low-grade glioma), third-degree astrocytoma (anaplastic astrocytoma) and fourth-degree astrocytoma (glioblastoma or malignant glioma).[1,2]

Brainstem gliomas account for 10%–20% of pediatric and less than 2% of adult brain tumors.[3-5] Approximately 80% of those tumors are diffuse intrinsic (high-grade) gliomas, originating inside the pons, and are related to a uniformly terrible diagnosis.[6-8] In contrast, most nonpontine tumors are low-grade gliomas. These tumors observe a greater indolent course, commonly arising inside the midbrain or medulla, with both a properly circumscribed (focal) look on MRI and much extra favorable diagnosis than diffuse brainstem gliomas.[5,6,8]

The treatment of brain tumors by brachytherapy was started in 1960 by Manderger. He used Ir-192 source for this purpose, but in 1979 he discovered that using I-125 source instead of Ir-192 gave a better response to the disease. Using iodine sources has become very popular in the treatment of brain tumors around the world. The usual method for implanting iodine sources in the brain is the stereotactic method. Also, more than 80% of glioma recurrences are within 2 cm of the site of origin, leading to the advent of stereotactic techniques for better radiation doses at the tumor's epicenter at the same time as sparing the surrounding brain.[9,10]

Stereotactic brachytherapy has been applied as an option for intrinsic brain tumors in numerous patients with glioma brain tumors in the past four decades.[11,12] Several reports and essays on various technical aspects of low-grade glioma tumor treatment have been studied in recent years.[13-18] The dose reached to the tumor and the sensitive organs around it is the most important parameter in cancer treatment. In brachytherapy, the arrangement of sources and seed time estimate the absorbed dose. In the present study, I-125 seed time and absorbed dose from Iodin-125 seeds for low-grade glioma tumor treatment was calculated at the border of tumor and healthy tissue using GATE code simulation.

Materials and Methods

Iodine-125

Radioactive iodine has long been used for medical purposes. Also, iodizing compounds is used in medicine and biology. Iodine-125 is customarily utilized for constant intracranial brachytherapy, however, Iodine-125 has come beneath grievance due to its almost long half-life (59.4 days) and for concern that resection cavity remodeling over time might mar nearby management and boost radionecrosis.[14,17] In this way, the rate of radionecrosis with permanent I-125 brachytherapy for brain metastasis has been mentioned to be as excessive as 23%.[18] I-125 source model is designed by Amersham company and approved by the American Physicians Association. The range of photons emitted from this source is 22-35 (KeV) and is produced in two stages in the nuclear reactor. In the first stage, Xe-125 gas enters the core of the nuclear reactor and is bombarded with high-energy neutrons, which, by absorbing neutrons, become the unstable radioisotope of Xe -125, which decays into I-125 by electrons decays. The beta spectrum emitted from the source can be ignored because the beta particles are not able to pass through the titanium shell of the source. The half-life of this isotope (I-125), which decays by electron captures, is 59.4 days.[19] Figure 1 shows a view of the I-125 seed of the once seed model.

The GATE Code

GATE code is a Monte Carlo simulation method that is potentially beneficial for a large variety of simulations, which includes the ones where the absorbed dose is the major observable.[20] GATE is a simulation code that is based on the GEANT4. While GATE presents extra high-stage capabilities to simplify the plans of GEANT4 simulations, GEANT4 manipulates the kernel that simulates the interactions. GATE code was advanced by the OpenGate collaboration and is a community driven initiative where anyone can access the source code and promote new characteristics.[21,22]

In this study, first, MRI images of the head of a patient with low-grade glioma were obtained and processed to store in the code as phantom voxels that could be used in the GATE code. It should be noted that the half-life of I-125 is 54 (days), which provides enough time to use it. Hence, there is no concern about lowering the dose rate during the treatment with radionuclides**.** Dosimetry characteristics of this isotope were defined by the updated TG-43U1 recommendations. In the next step, MRI images were given to MATLAB software so that the tumor was contoured on the MRI images and the phantom of the brain contained the segmented tumor (Figure 2). Finally, the contoured file is passed to the XMedCon software (an open source toolkit for medical image conversion)[23] to create the input file to extract the Interfile for Gate 20 (MBq) activity. Finally, the absorbed dose at the border of the tumor and healthy tissue were calculated. Figure 3 shows a dose view on MRI images for a different number of seeds.

Results

The usual method of treating a brain glioma tumor is to implant a radioactive source in the center of the tumor. In this study, first, 18 MRI images of two patients with tumor sizes of 3 and 5 cm were prepared. Each image has a 256 * 256 matrix with pixels of 0.94 * 0.94 mm and a thickness of 5 mm, which covers the tumor and its surroundings completely. Also, in this paper, in addition to simulation of one radioactive source (iodine-125) seed design, the results of two and four radioactive source seed designs were checked (Figure 4). It is necessary to mention that the distance between the centers of both simulated

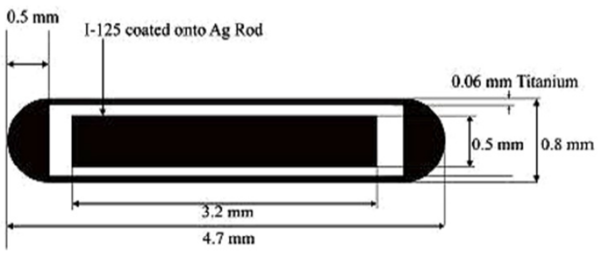

Figure 1. I-125 Seed Onceseed Model Scheme.

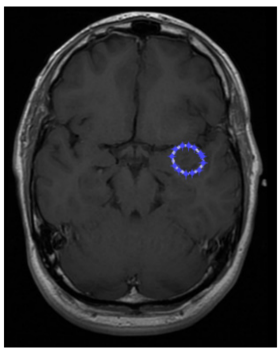

Figure 2. Contoured Image in MATLAB Scheme.

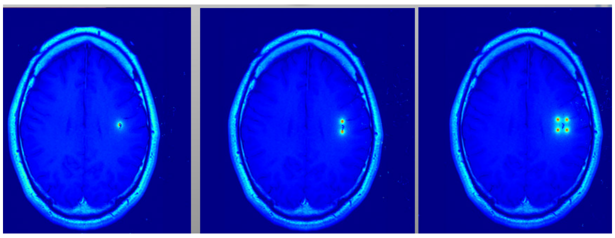

Figure 3. Dose View on MRI Images for Different Number of Seeds.

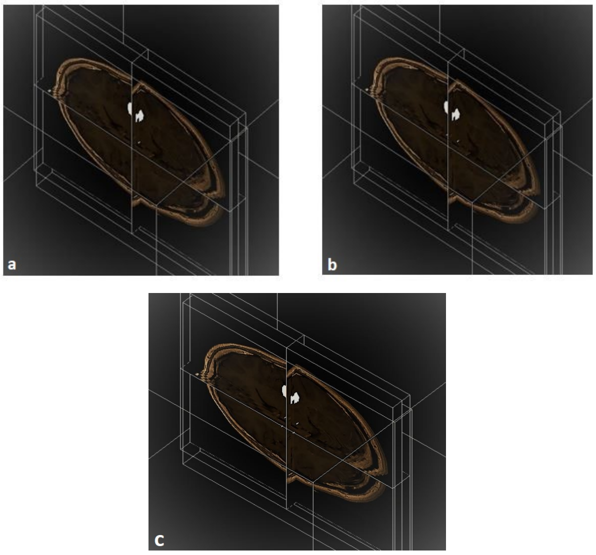

Figure 4. Simulation of Iodine-125 Sources in the Brain Tumor, (a) One Seed, (b) Two Seeds, (c) Four Seeds.

radioactive sources in the brain was 1 cm.

The dose reached to the tumor and the sensitive organs is the most important parameter in the cancer treatment. In brachytherapy, the amount of dose depends on the arrangement of radioactive sources and seed time. According to GATE code data and Eq. 1 time seed (T) of radioactive sources will be achieved, as follows:

$$T = T_{1/2} / \ln 2 \, [\ln (1 - (\ln 2 / T_{1/2}) * (D / \dot{D}))] \qquad (1)$$

Where $T_{1/2}$ is half life of iodine-125 radioactive source in days. Also, D and $\dot{D}$ are the absorbed dose and absorbed dose rate in units of (cGy) and (cGy/day), respectively. It should be noted that absorbed dose rate obtained from GATE code calculations. However, the absorbed dose parameter is the prescribed dose for the patient equivalent to 6000 cGy.

In this study, calculations were done once for the two tumors with sizes of 3 and 5 cm. Also, results using the GATE code have an uncertainty of less than 5% in body tissues. Hence, the results have an appropriate consistency. Absorbed dose rate at the border of tumor and healthy tissue obtained from GATE code for both tumor sizes of 3 and 5 (cm) are shown in Table 1.

According to the absorbed dose rate results from GATE code, I-125 seeds time is calculated (Eq. 1) and shown in Table 2.

Table 1. Absorbed Dose Rate Per one Becquerel (Bq) Per One Second at the Border of Tumor and Healthy Tissue

Number of Sources	Absorbed Dose at the Boundary of Tumor (cGy/Bq.sec)	
	3 (cm)	5 (cm)
1	3.50 E -5	1.77 E -5
2	4.00 E -5	3.82 E -5
4	9.80 E -5	7.85 E -5

Table 2. I-125 Seeds Time Calculation

Number of Sources	Seed Time (Day)	
	3 (cm)	5 (cm)
1	115	170
2	83	90
4	62	69

Absorbed dose distribution in the brain tumor for one, two and four seeds are demonstrated in Figures 5 to 7.

Discussion

In this study, GATE code simulation has been used by the Gate code with 20 MBq activity for an iodine seed design for low-grade glioma tumor treatment. According to data, the ideal form for brachytherapy is for tumors smaller than 4 cm. Also, the larger the tumor size, the absorption dose at the border of tumor and healthy tissue will be decreased. On the other hand, the implantation time for iodine seeds will increase. Hence, it is recommended this brachytherapy treatment be proposed for tumors size smaller than 4 cm. The reason is that, for larger tumor size, the number of sources must increase and the risks of radiation for organs at risk will ascend. On the other hand, since the most important goal in tumor treatment is to reach the highest dose to the tumor and the lowest dose to healthy tissues, the treatment time increases exponentially according to the size of the tumor and the surrounding organs will be more damaged, respectively.

According to the calculations, placing an iodine-125 source inside the tumor is not sufficient due to the non-uniform dose distribution in the tumor and the length of treatment time. By placing two iodine-125 sources in the tumor, the treatment time will decrease, but again, this is not appropriate due to the non-uniformity of dose distribution in the tumor. Finally, the placement of four iodine-125 sources eliminates the tumor, and also, a uniform dose distribution is created in the tumor and the implantation time will be reduced. Hence, the effectiveness of treatment will be greater.

Comparison of the results of this study with previous reports shows an appropriate consistency. There was a slight difference between the results related to the calculation method; in this study the Monte Carlo method was used. However, in previous papers, experimental methods have generally been performed with some assumptions.[16]

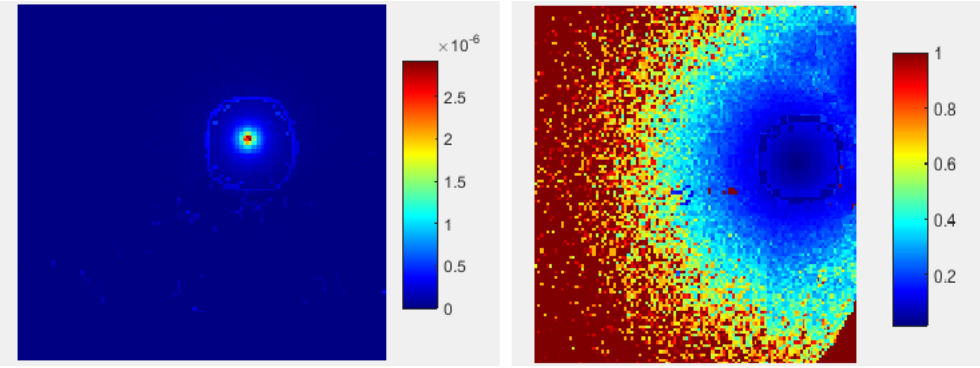

Figure 5. Absorption Dose Distribution in the Brain Tumor for One Seed.

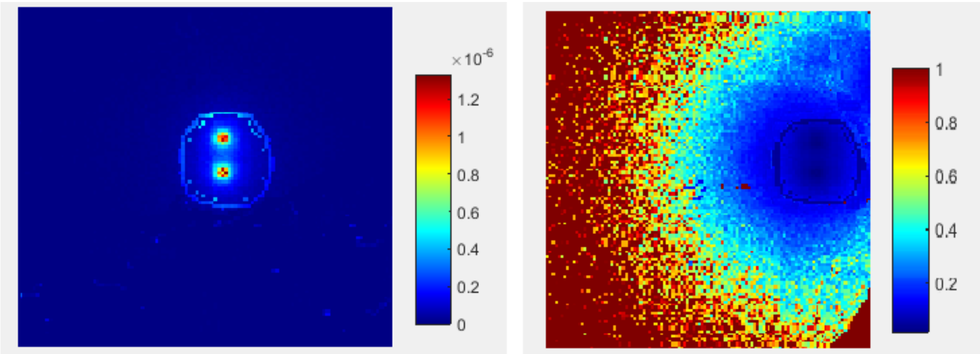

Figure 6. Absorption dose Distribution in the Brain Tumor for Two Seeds.

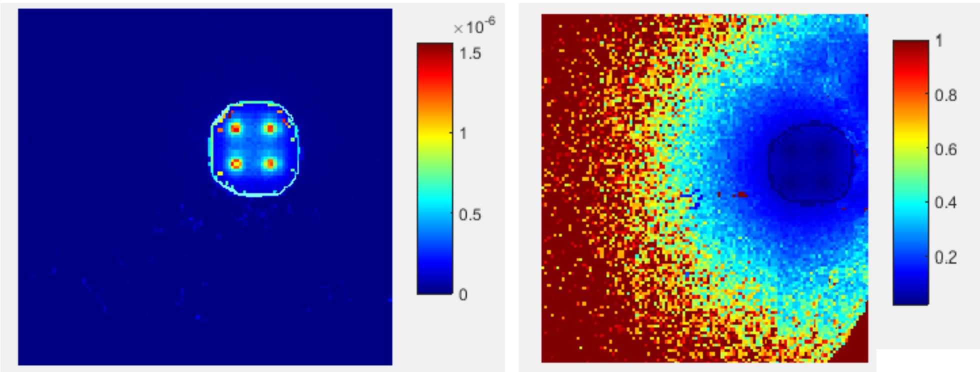

Figure 7. Absorption Dose Distribution in the Brain Tumor for Four Seeds.

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Conflict of Interest Disclosures

The authors declared that they have no conflicts of interest in this paper. Also, we declare the following financial interests that represents a conflict of interest in connection with the research works submitted.

Ethical Statement

The authors of the article certify that all ethical principles related to research have been completely met. The local ethics committee of the science and research branch has approved the study (Code: 317088).

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