Artificial intelligence-based solution for bioluminescence tomography reconstruction for glioblastoma multiforme

Document status and date:
Published: 01/01/2024

DOI:
10.26481/dis.20240123br

Document Version:
Publisher's PDF, also known as Version of record

Summary

According to the World Health Organization (WHO), nearly one in every six deaths worldwide is due to cancer, making it the number one death cause worldwide. Treating cancer is different for each person, and it depends on the type of cancer and how advanced it is. But for almost half of all cancer patients, a treatment called radiation therapy or radiotherapy is used at least once. This treatment option uses strong ionizing radiation to target tumor cells. Ionizing radiation will damage the targeted body tissue, and with strong enough radiation, i.e. high radiation dose, it can even kill the cells inside the tissue. Therefore, the main goal of every radiation therapy is to target and destroy the tumor cells with high-dose ionizing radiation with minimum effect on the rest of the healthy cells and tissue.

In recent years, technological advances have enabled clinicians to use various techniques to target tumors with radiation more effectively and make radiotherapy an efficient treatment for most tumor types. However, some tumors are more resistant to ionizing radiation or reappear after a short period. Glioblastoma, the most common and aggressive brain tumor, is one of such tumors that do respond well to the standard treatment, which includes a combination of radiation therapy and chemotherapy. Biologists have identified theoretically various reasons for this, but these hypotheses must be tested completely before translating into a clinical treatment option. Therefore, there is a need for a testing environment, namely preclinical research, that allows for fundamental research investigation and identifying new treatment options to ensure the safety of patients.

Preclinical cancer research tries to improve the quality of the standard treatment options, with otherwise low survival rates, such as glioblastoma, by investigating novel ideas and hypotheses. In this field of research, new ideas are first tested in the lab environments on tumor cells growing in plates, and the treatment efficacy is monitored under the microscope. The next step is to ensure that the tumor cells behave similarly in the vicinity of other body tissues to ensure the same result in the human case. Therefore, the tumor cells are implanted inside small animals such as mice and rats and investigated even further. Since the clinical imaging and radiation therapy systems are too big for such small objects, a new field of research emerged, which resulted in commercially available imaging and radiotherapy systems dedicated to small animals.

Small animal radiotherapy is a field of research that is very analogous to the routine clinical workflow. In other words, the animals are first imaged using a computed tomography (CT) system to identify the location of the tumor and then irradiated using X-ray radiation to destroy them. However, the dimensions of the animals and tumors in small animal radiotherapy are much smaller than the dimensions in humans, hence requiring a much higher precision and resolution. This increased

resolution often causes the CT imaging in the small animal to deliver a higher X-ray radiation dose during the imaging process, namely the imaging radiation dose. Additionally, when it is considered together with the lower tolerance of small animals to ionizing radiation, it underlines the necessity of a novel imaging technology that can identify the location and shape of the tumors without radiation burden on the animals.
Bioluminescence Imaging (BLI) is an imaging technique that uses the same biological process from a firefly to locate the tumor. In other words, the tumor cells are modified in the lab to emit visible light, similar to a firefly. In practice, these modified tumor cells are activated when a substrate is present in their vicinity and will emit light. Once the modified tumor cells are placed inside the animals, after the injection with the corresponding substrate, only the modified tumor cells will light up. Thereafter, the emitted light will travel through the surrounding tissue and leave the animal's body. By this time, the emitted light will be not only diffused but also reduced in intensity due to the surrounding tissue. However, a very sensitive camera can still see this light in a very dark cabinet and create the BLI images, which corresponds well with how big the tumor is. This imaging technology can provide helpful information about the effect of each treatment option, especially radiation therapy, on the tumor cells by looking at the changes in the emitted light over the course of the treatment. However, this technique is not applicable for human subjects since it includes tumor cell modification and injection of a substrate borrowed from firefly.
BLI is used in preclinical cancer research daily to monitor tumors' response to various treatments and determine which treatments are more effective for different tumor types. However, the BLI ability is limited to tumor growth monitoring, and it cannot be used for targeting the tumor cells with X-ray radiation. Therefore, a high-dose CT scan is still needed to obtain the placement of the tumor and obtain a radiotherapy treatment plan, which finds the best arrangement of X-ray radiation beams that deliver the highest radiation dose to the tumor cells and the lowest possible radiation dose to the healthy tissue. In other words, the studies that want to investigate the role of X-ray radiation in cancer treatment cannot employ BLI as their imaging technique and must use a high-dose CT scan with previously mentioned limitations.
This thesis aims to obtain the tumor placement in three dimensions (3D) using the information provided by the BLI and, therefore, enabling the use of the BLI for preclinical cancer research in small animal radiotherapy, specifically for glioblastoma. Here, to obtain the required 3D information from the 2D BLI images, a series of novel Artificial Intelligence (AI) approaches are developed that can accurately predict the tumor's location inside the animal. The developed techniques in this thesis can locate the tumor within a millimeter of its actual location. Furthermore, the Dice similarity coefficient is routinely used to objectively measure the quality of tumor segmentation in medical imaging, which scores the overlap

between the actual and the predicted tumor. The developed methods in this thesis can achieve an average Dice score ranging from 62 to 83% depending on the available information and the type of the employed AI model. Therefore allowing the biologists to target the investigated tumor cells using BLI.