Automatic Motion Management with Biology-guided Radiotherapy

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BACKGROUND

Advances in radiotherapy, including treatment techniques such as intensity-modulated radiation therapy (IMRT) and stereotactic body radiotherapy (SBRT) improve dose delivery and conformity, but managing motion during treatment, especially in moving tumors, remains a challenge. To manage motion, radiotherapy currently relies on anatomical imaging and surrogates including the use of fiducials or external markers to approximate the location of the tumor. With biology-guided radiotherapy (BgRT)\(^1\), the paradigm is reversed with the tumor itself continuously signaling its location to actively guide treatment beam delivery. As the cancer’s own biology in effect drives the treatment in real-time, motion management becomes automatic. Furthermore, with a single administration of a PET radiotracer “lighting up” tumors in multiple locations in the body, BgRT may one day enable motion-managed treatment of multiple tumors in the same session.

PURPOSE

This paper aims to depict how BgRT manages and accounts for tumor motion, and to describe the differences between BgRT motion management and traditional radiotherapy techniques.

TRADITIONAL MOTION MANAGEMENT

To manage motion, radiotherapy relies on the use of anatomic imaging, gating, fiducials, or external markers. Respiratory gating is a breathing technique that uses software and a device to monitor breathing and adjust the radiation beam during treatment as needed. It is used routinely, for example, in lung stereotactic body radiotherapy. While gating has proven helpful for sparing healthy tissue, it can increase treatment time and may be challenging for some patients particularly for those with reduced lung capacity.

Given that traditional radiotherapy uses anatomical imaging taken days before treatment, fiducials or surface monitoring devices are needed to accurately determine tumor location at the time of treatment. However, fiducials are implanted invasively\(^2\), requiring local anesthetic and can create patient discomfort during and after the procedure; they may also drift throughout the course of treatment\(^3\).

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\(^1\) The RefleXion® X1 is cleared for SBRT/SRS/IMRT. BgRT is pending regulatory review and it not commercially available.


Unlike either gating or fiducials, BgRT relies on signals from the cancer itself to determine where beamlets of radiation are delivered during treatment. Once given authorization by the U.S. Food and Drug Administration (FDA), BgRT will remove the need for gating or fiducials and create a simplified and universal motion management solution using injected radiotracers that can account for the motion of a moving tumor.\(^4\)

**BGRT OVERVIEW**

BgRT is a novel radiotherapy modality that relies on emissions generated by an injected PET radiotracer to guide the radiotherapy beam during each fraction. As a result, BgRT allows for real-time, tracked dose delivery to tumors that are subject to motion. The combination of positron emission tomography (PET) and radiotherapy, in a single machine, brings a paradigm change to conventional image-guided radiotherapy techniques.

**FIGURE 1: Dual PET arc detectors on the RefleXion® X1**

![Dual PET arc detectors on the RefleXion® X1](image)

Figure 1. Demonstrates where the two 90-degree PET arcs have been built into the RefleXion X1 system.

**LIMITED-TIME SAMPLED IMAGES**

During treatment, the gantry continuously rotates around the target at 60 RPM acquiring emissions and grouping them to form limited time sampled (LTS) PET images. The data contained in each LTS image guides a portion of fluence delivery (partial fluence). The RefleXion X1 calculates fluence at 10 frames/second to create machine instructions to control beam delivery. This fast rotation allows the

\(^4\) Initial initial FDA authorization will be for use with the radiotracer FDG. Subsequent novel tracers will require separate FDA review.
X1 machine to capture and process these LTS data sets before the tumor has significantly changed position. LTS images are transformed to fluences that gradually build to match the planned dose. At the end of delivery, the LTS images have summed up to create the full PET image, and the partial fluences have summed to complete the intended fluence or dose.

**FIGURE 2: Sample LTS image formation and dose delivery on the RefleXion X1**

![Diagram of LTS image formation and dose delivery](image)

*Figure 2.* Demonstrates the formation of a full PET image at the end of treatment as well as the full dose delivered.

**ACCOUNTING FOR TUMOR MOTION DURING BGRT TREATMENT PLANNING**

**Imaging-only Session**

A unique part of the BGRT treatment planning workflow includes an imaging-only session. During this step, the patient is injected with a radiotracer, similar to that on the day of treatment. This session characterizes the tumor based on the PET image and enables the X1 machine to understand the characteristics of the tumor and account for any varying intensity of PET signals in the background. This imaging-only session approximates what the LTS PET images and resulting partial fluences will be during treatment. The data from the imaging-only session will be used by the X1 treatment planning system to generate a BGRT treatment plan that then can be approved by the clinical team.
Dose Tracked Delivery with BgRT

During dose delivery, BgRT effectively tracks a smaller planned tumor volume (PTV) as predetermined in the treatment plan compared to IMRT/SBRT. The BgRT delivery process uses the characteristics of the real-time LTS images to keep the dose on the moving target. Because the dose tracks the PTV, the ability to deliver the prescribed dose is not dependent on PET radiotracer uptake to all areas of the tumor. As an example, the tumor may have a region or regions without PET activity, while the treatment plan may prescribe dose to all regions of the tumor, including those without activity. Even if the PET depicts a shape that varies from that of the shape delivered, the expected dose delivery will still occur as planned – even while the tumor is in motion.

Biology-tracking Zone

In contrast to the conventional SBRT PTV, which is fixed relative to the patient anatomy, the BgRT PTV moves within a pre-defined biology-tracking zone (BTZ), an area unique to BgRT defined by the radiation oncologist at the time of treatment planning. The BTZ encompasses the entire motion envelope of the tumor, but it is not a prescription volume. Rather, it acts as a safeguard and only structures producing a PET signal from within the BTZ will be targeted. PET signals arising from outside of the BTZ are still collected but will not guide delivery. It is important to note that while radiation delivery can occur anywhere within the BTZ, dose delivery is only prescribed to the moving PTV.

Figure 3. Illustration demonstrates the biology-tracking zone that will account for motion and the smaller PTV where dose is prescribed.
A distinct feature of the BgRT treatment planning is that it generates a continuum of possible radiotherapy dose distributions that reflect variations in tumor position and tumor contrast, visually represented below in a bounded dose–volume histogram (bDVH). Specifically, different positions of the tumor within the BTZ as well as variations of contrast up to 25% are modeled. This distinct feature of BgRT robustly accounts for and models the likelihood that the tumor’s behavior and appearance at each treatment fraction may change by a limited amount. During treatment planning, the physician approves the comprehensive set of dosimetric scenarios represented by the bDVH that can occur during BgRT delivery.

FIGURE 4: Illustrated Bounded Dose-Volume Histogram

Figure 4. Demonstrates the bDVH that accounts for variations in tumor position and contrast modeled prior to treatment.

Treatment Day Verification

The treatment workflow for each BgRT fraction incorporates a verification step (PET pre-scan and evaluation) prior to delivery that checks whether the observed PET activity on the day of treatment falls within the continuum of modeled PET variations. The PET pre-scan is a short PET scan performed on the RefleXion X1 machine.

BgRT Experimental Validation

A multitude of experiments have been conducted to validate the BgRT delivery process. One such experiment involved simulating a moving tumor with a sphere filled with a PET tracer (FDG) in a bath of lower activity FDG and placing the apparatus on a moving stage. Non-periodic realistic breathing motion was used to move the spherical target. X-ray film was placed inside the sphere to

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measure the radiation dose from the target's point-of-view. Three deliveries were conducted: standard SBRT (i.e., with BgRT turned off) with the target moving, BgRT with the target stationary, and BgRT with the target moving\(^6\). The results demonstrate that not only was the desired dose delivered to the target as planned, but BgRT is able to deliver the prescribed dose with a smaller PTV. In this study, tracked dose delivery demonstrates better conformality and normal tissue sparing than free breathing techniques where the entire internal target volume (ITV) receives radiation.

**FIGURE 5: Plan vs actual delivery measured on film comparing SBRT with motion (left panels), BgRT without motion (center panels), and BgRT with motion (right panels).**

<table>
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<th>TREATMENT TECHNIQUE</th>
<th>PLAN CTV MIN DOSE (%)</th>
<th>MEASURED CTV MIN DOSE (%)</th>
<th>PLAN CTV MAX DOSE (%)</th>
<th>MEASURED CTV MAX DOSE (%)</th>
<th>CTV DOSE COVERAGE MET?</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBRT (MOTION)</td>
<td>97.0</td>
<td>104.0</td>
<td>132.5</td>
<td>123.8</td>
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<tr>
<td>BgRT (STATIC)</td>
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<td>109.3</td>
<td>117.6</td>
<td>126.1</td>
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<tr>
<td>BgRT (MOTION)</td>
<td>97.0</td>
<td>121.5</td>
<td>147.1</td>
<td>139.9</td>
<td>YES</td>
</tr>
</tbody>
</table>

The criteria included dose coverage where 100% of the clinical target volume (CTV) receives at least 97% of the prescription dose and maximum dose in the CTV was $\leq 130\%$ of the maximum planned dose.

*Results scaled to enable comparison from those cited in the reference below*

**BgRT Margins Compared to Traditional Motion Management**

For traditional motion management in the lung or the body, the recommended effective margin as indicated by ICRU Report 50 and 62 is a 5mm internal target volume (ITV) to planned target volume (PTV) expansion. With BgRT delivery, the recommended margin is 5mm clinical tumor volume (CTV)
to PTV expansion. The 5 mm BgRT margin comprises a 2mm imaging-only margin (RefleXion PET-CT to the simulation-CT) plus a 3mm BgRT tracking margin. The CTV is not expanded to include the motion of the tumor as compared to an ITV as demonstrated in Figure 5 above. The BgRT tracking margin has been bench tested for respiratory and non-respiratory cases including periodic and non-periodic motion.\(^6\)

**BREAKTHROUGH DEVICE DESIGNATION**

BgRT’s novel approach to managing motion recently earned it Breakthrough Device designation by the U.S. Food and Drug Administration (FDA) for use in treating lung tumors. The FDA Breakthrough Devices Program recognizes medical devices that meet certain criteria and hold the potential to provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating disease or conditions. The breakthrough potential of BgRT lies in its ability to detect emissions and treat tumors with sub-second latency.

**CONCLUSION**

RefleXion BgRT is the first to utilize the cancer itself to guide radiation delivery - even in tumors that are moving. BgRT will remove the need for gating or fiducials as the tumor itself is signaling its location and guiding treatment beam delivery. RefleXion BgRT envisions a leap forward in the ongoing goal of managing motion, reducing margins, and diminishing toxicity, so that one day multiple tumors can be treated in parallel during the same session.