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Title:

Preliminary analysis for integration of spot-scanning proton beam therapy and real-time imaging and gating

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Abstract

Purpose:

Spot-scanning proton beam therapy (PBT) can create good dose distribution for static targets. However, there exists larger uncertainty for tumors that move due to respiration, bowel gas or other internal circumstances within the patients. We have developed a real-time tumor-tracking radiation therapy (RTRT) system that uses an X-ray linear accelerator gated to the motion of internal fiducial markers introduced in the late 1990s. Relying on more than 10 years of clinical experience and big log data, we established a real-time image gated proton beam therapy system dedicated to spot scanning.

Materials and methods:

Using log data and clinical outcomes derived from the clinical usage of the RTRT system since 1999, we have established a library to be used for in-house simulation for tumor targeting and evaluation. Factors considered to be the dominant causes of the interplay effects related to the spot scanning dedicated proton therapy system are listed

and discussed.

Results/Conclusions

Total facility design, synchrotron operation cycle, and gating windows were listed as the important factors causing the interplay effects contributing to the irradiation time and motion-induced dose error. Fiducial markers that we have developed and used for the RTRT in X-ray therapy were suggested to have the capacity to improve dose distribution. Accumulated internal motion data in the RTRT system enable us to improve the operation and function of a Spot-scanning proton beam therapy (SSPT) system. A real-time-image gated SSPT system can increase accuracy for treating moving tumors. The system will start clinical service in early 2014.

Keywords

gated radiotherapy, organ motion, image-guided radiation therapy, spot-scanning proton beam therapy

Introduction

Proton beam therapy (PBT) has the potential to provide better dose distributions to the target being treated and reduce the dose to the target at risk (OAR) than X-ray therapy in many situations [1]. Spot-scanning proton beam therapy (SSPT) is expected to be more suitable to create more complex dose distributions to the target volume and also expected to be safer in terms of reducing the neutron contamination [2]. The SSPT has been considered disadvantageous to the conventional passive scattering PBT because of larger uncertainty in the dose distribution for the moving target due to interplay effects. The existence of the internal motion mainly from respiration is an issue to be discussed when we consider using the SSPT especially to treat lung and liver tumors.

We developed the real-time tumor-tracking radiation therapy (RTRT) system in 1999 and have been using it in the X-ray clinic for over 10 years [3]. The system can gate therapeutic x-rays according to the internal location of a fiducial in or near the tumor. The 3D trajectory of the fiducial marker is observed and calculated 30 times per second. We have started to develop a spot-scanning dedicated PBT system integrated with the RTRT system. The aim of this integration is to accurately treat tumors with SSPT that

have respiratory movement. As the internal motion of lung and liver tumors is often different from the external surface motion of the chest or abdominal wall [4], it is insufficient to use surface motion for accurate estimation of target motion. In this study, a real time 3D fiducial location database obtained from the clinical experience using the RTRT system is used for simulation study of SSPT.

Materials and methods

Two orthogonal sets of X-ray fluoroscopes are installed in the gantry of the system to observe internal fiducials or bony structures before and during the beam delivery (Fig. 1). As an SSPT system does not require compensators and collimators, the X-ray images can be acquired simultaneously with proton beam irradiation at any beam angle, and their fields of view will not be narrowed by these field-shaping devices. The system supports the gating function of the therapeutic beam to the real-time image of a fiducial marker. In this study, we estimated how much dose uncertainty may be reduced through usage of real-time image gating compared to free-breathing.

Using the log data and the clinical outcomes derived from the clinical usage of the

RTRT system since 1999, we have established a library of 3D fiducial location movement data for the various kinds of diseases and locations to be used in simulation for tumor targeting and evaluation. The log file of the RTRT system derived from its clinical usage holds various parameters including marker locations, and recognizing score and system information such as the beam triggering signal. Also, the data sometimes contain short periods indicating that the system has lost the marker location or there is accidental noise; we excluded data sets that are not suitable for this SSPT simulation study (Fig 2). In Hokkaido University Hospital, we selected 78 patients' 397 trajectory data sets that serve as the library of tumor movement. The trajectory data are called "Hokkaido data" in this study.

Using the Hokkaido data, a new function for the synchrotron operation optimized to spot-scanning with gating technique was developed in order to improve the beam efficiency. This function enables the multiple gate irradiations per operation cycle of the synchrotron. During the flat top phase of the synchrotron, even if the sequential spot irradiation is halted due to the gate-off, it can be resumed if the marker returned to the

gating window, which was defined as the permitted displacement of the marker from the planned position, within a time limit of 200 ms.

In this study, the in-house simulation tools were used for estimating the dose distribution. A gated proton beam was irradiated to a clinical target volume (CTV) of 5 $\times 5 \times 5$ cm^3 in a water phantom, in synchronization with the tumor trajectory log of the Hokkaido data. The gating window was set to ± 2 mm based on previous simulation study [5]. The plan was constructed to deliver a 2 Gy dose to the internal target volume (ITV), which was defined as CTV + 5 mm. Other factors contributing to the uncertainty in dose delivery, e.g., positioning errors, CT number uncertainty, and dose calculation algorithms, were not explicitly considered. The depth of the target ranged from 15 to 21 cm. We predicted the maximum dose error within the CTV due to tumor motion and compared it between free breathing and gating during spot-scanning proton therapy.

Results

Three factors are considered to be the main problems in developing a SSPT dedicated gating system from our imaging perspective and comparison with our experience of

photon treatment through the clinical usage of the RTRT system. They are 1. synchrotron operation cycle, 2. gating window, and 3. precise targeting.

1. Synchrotron operation cycle is a new factor that was not a problem when we developed the RTRT system for x-ray therapy. For the integration of SSPT and RTRT, we realized that the relationship between synchrotron operation cycle and the respiratory cycle should be investigated beforehand. Otherwise, the interplay effects cannot be reduced without large prolongation of treatment time by the integration of SSPT and RTRT.
2. Gating windows for the fiducial marker have been +/- 2 mm in RTRT with x-ray therapy. For SSPT, we realized that the appropriate gating windows should be determined beforehand to reduce the interplay effects; thereby, avoiding extensive prolongation of treatment time.
3. Theoretically, gating the SSPT system to the real-time imaging of an internal fiducial marker can reduce localization error. A simulation study was conducted to see the efficacy of gating in SSPT (Fig. 3). Based on the log data of 78 patients, real-time image gated SSPT was suggested to suppress the maximum dose error

to less than 5% against the prescribed dose with the gating windows of +/- 2 mm (Fig. 4). The incidence of the number of the patient that the dose error exceeds over 5% is only 5 patients (6.4%) with the use or real-time image gating in SSPT. But without gating the number increase into 16 patients (20.5%). And the maximum dose error is 6.7% with gating can be increased into 26.6% without gating.

Discussion

SSPT is considered a promising system that can deliver to the target volume high dose conformity with reducing secondary neutron dose and realizing a reduction of the total facility size [6]. Existence of interplay effects, however, during beam delivery is considered to be one of the important problems to perform SSPT clinically. In the present study, we investigated the relationship between the organ motion and SSPT. The details of the analysis of the internal motion of fiducial markers can be more useful in the evaluation of interplay effects in SSPT [5]. Another problem with the gating method is the possibility of its prolonging the treatment time. Various methods and parameters

are considered through the simulation study using the “Hokkaido data”.

The conventional PBT system has required scattering filters and collimators in the gantry. Thus, it was difficult to install fluoroscopic devices for real-time orthogonal imaging during PBT. A SSPT dedicated system is designed not to require compensators and collimators. Therefore, the SSPT dedicated system enables two orthogonal X-ray tubes and FPD panels to be installed beside the nozzle within the gantry. These two orthogonal imaging units can be used for the real-time fluoroscopy during SSPT. This imaging device can be used for patient setup and also for RTRT function to gate the therapeutic beam to the real-time imaging of a fiducial marker.

We showed +/- 2mm windows are considered to be appropriate enough in suppressing dose error, and our previous report also showed the +/- 2mm gating window is ideal in the point of view of dose uniformity and delivery time [5]. But further investigation is required for revealing the criteria to set individual gating windows. One of the shortcomings of the present study is that all the data are from simulation studies and not from clinical outcome using SSPT. Also, the time structure of the synchrotron is modeled based on specification given by the manufacturer, which may be

too simplified as compared to the actual system. The other shortcoming is that the simulation studies have been performed using rigid model, influenced by the small fiducial to the dose distribution [7], minute change around the tumor and fiducial, phase control of the log data and beam delivery in each simulation. The above are the main concerns that we need to address in the future.

Despite the aforementioned shortcomings, the simulation study was able to evaluate the impact from the spot-scanning beam delivery and the movement that manifest in the inner environment around the tumor and OARs. The tumor/target motion library that we established as “Hokkaido data” proved to be a useful tool to solve the three main problems in developing the SSPT dedicated gating system.

Conclusion

We are currently integrating the real-time tumor-monitoring system with the spot-scanning dedicated PBT system. Data from the RTRT system and its clinical use enable us to improve the operation and function of the PBT system and to decide the proper parameters. A proton beam therapy system dedicated to spot-scanning can

increase accuracy for moving tumors with real-time imaging and gating. The system will be introduced to clinical service in early 2014.

Conflicts of interest

Dr. Shirato has a patent “MOVING BODY PURSUIT IRRADIATING DEVICE AND POSITIONING METHOD USING THIS DEVICE” licensed to Hokkaido University, Japan. The other authors declare that they have no conflicts of interest.

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Figure legends

Figure 1.

Design of a spot-scanning proton beam therapy-dedicated system with X-ray fluoroscopy. Two orthogonal sets of X-ray fluoroscopic generators and flat panels can be mounted in the gantry.

Figure 2.

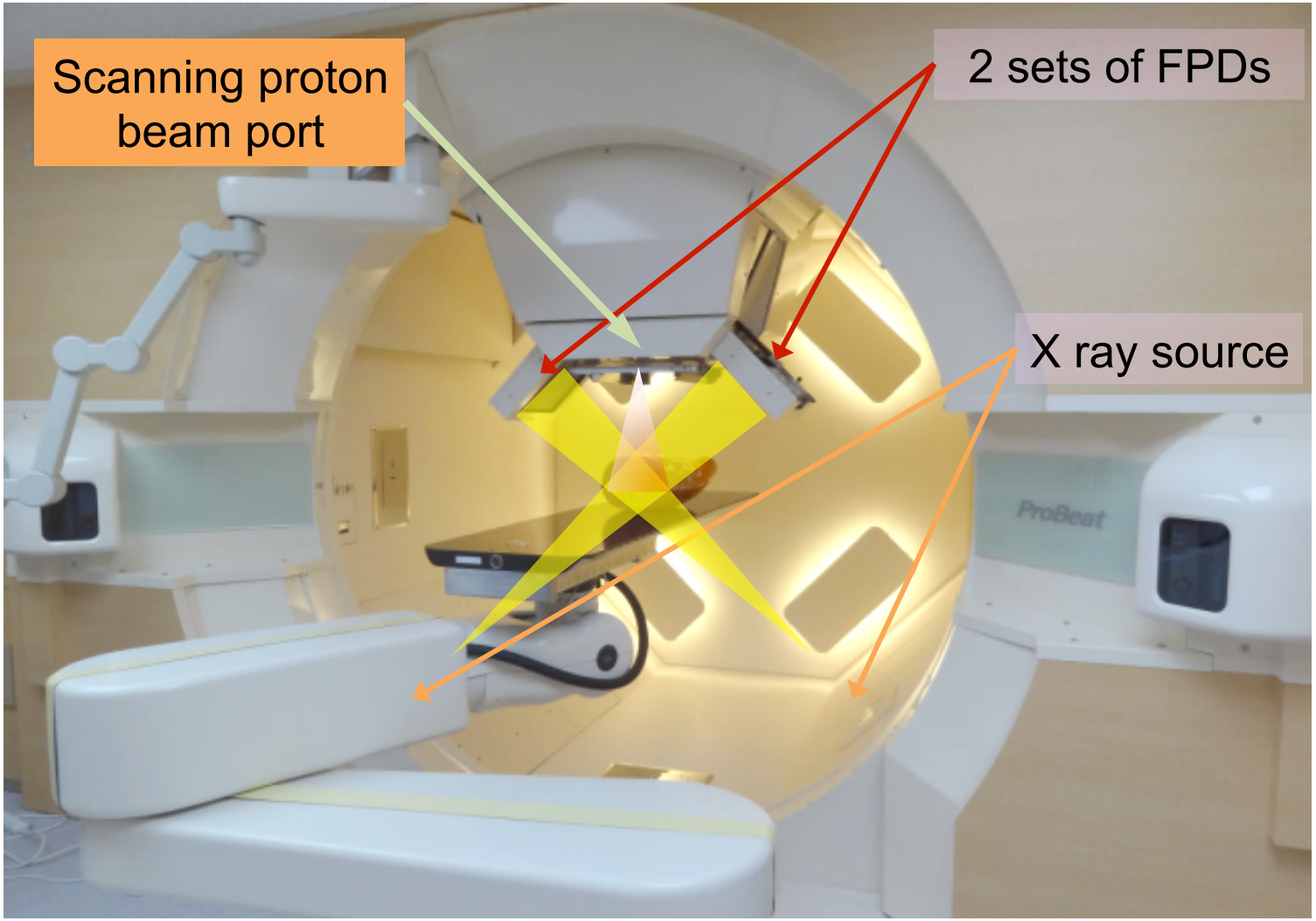
Selection of the tumor movement data from the RTRT log file. Some data sets contain incidental target loss during treatment.

Figure 3.

Example images of the dose distributions along the central beam axis with free-breathing (dotted curve) and gated spot-scanning proton beam therapy (solid curve).

Figure 4.

Summary of the improvement of motion induced dose error. Simulation results of the 78 patients 397 log data sets of tumor movement. Each green and red dot represents the tumor's maximum dose error within the target. Without gating, there exist lower doses within the target volume that are mitigated by gating.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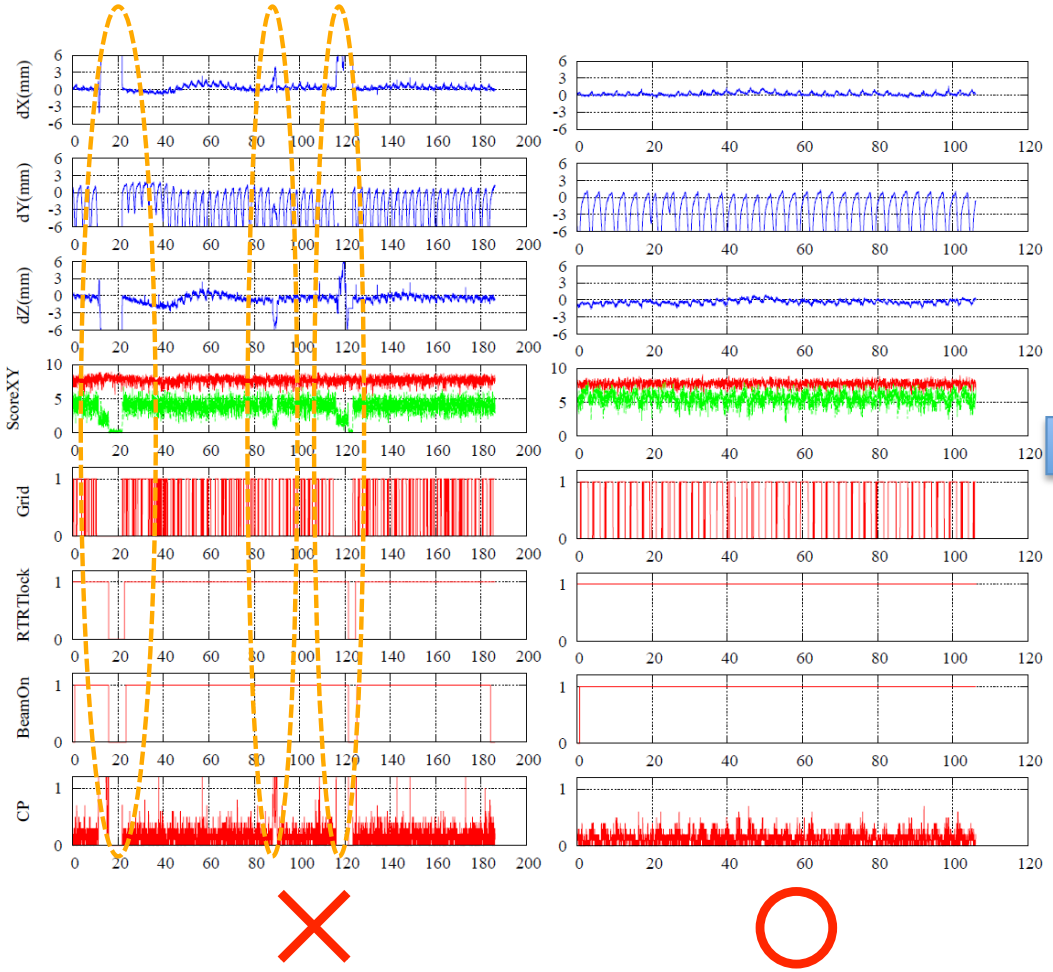
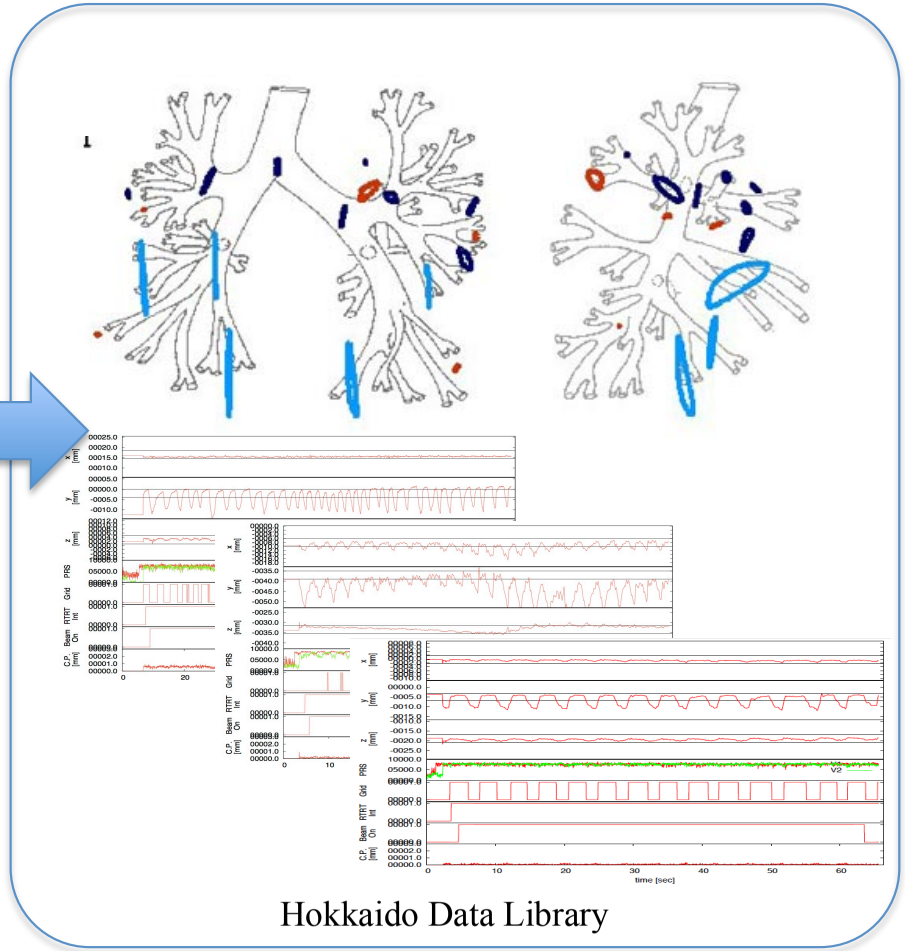
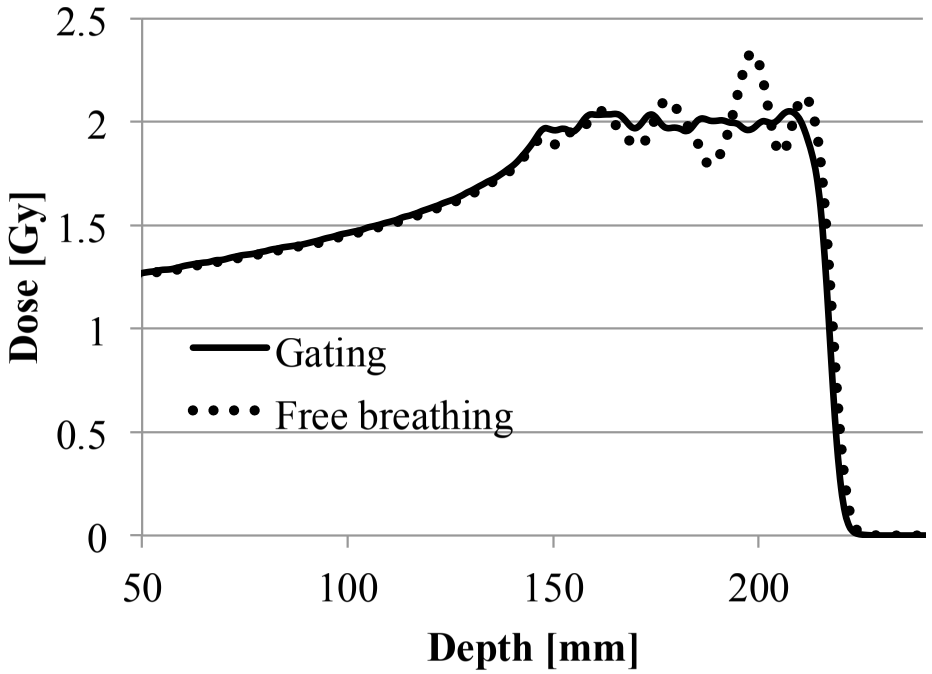
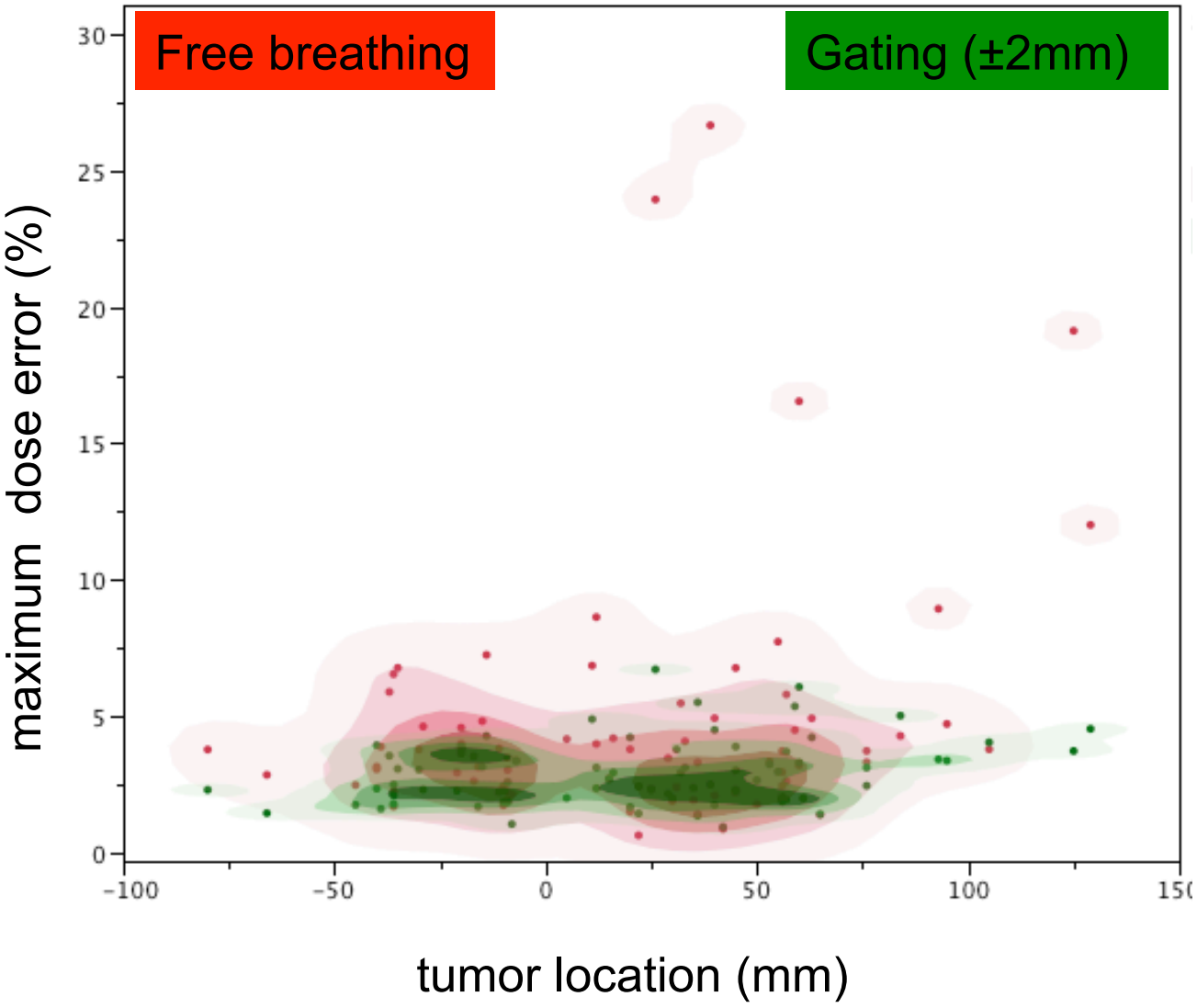
2 sets of FPDs
X ray source
ProBeat





Hokkaido Data Library


2.5
2
1.5
1
0.5
0
Dose [Gy]
Gating
Free breathing
50
100
150
200
Depth [mm]


Free breathing
Gating (±2mm)
maximum dose error (%)
tumor location (mm)
30
25
20
15
10
5
0
-100
-50
0
50
100