

The first clinical treatment with kilovoltage intrafraction monitoring (KIM): A real-time image guidance method

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ABSTRACT

Purpose: Kilovoltage intrafraction monitoring (KIM) is a real-time image guidance method that uses
20 widely available radiotherapy technology, i.e. a gantry-mounted x-ray imager. We report on the
geometric and dosimetric results of the first patient treatment using kilovoltage intrafraction
monitoring (KIM) which occurred on September 16, 2014.

Methods: KIM uses current and prior 2D x-ray images to estimate the 3D target position during
25 cancer radiotherapy treatment delivery. KIM software was written to process kilovoltage (kV) images
streamed from a standard C-arm linear accelerator with a gantry mounted kV x-ray imaging system.
A 120⁰ pre-treatment kV imaging arc was acquired to build the patient-specific 2D to 3D motion
correlation. The kV imager was activated during the megavoltage (MV) treatment, a dual arc VMAT
prostate treatment, to estimate the 3D prostate position in real-time. All necessary ethics, legal and
regulatory requirements were met for this clinical study. The QA processes were completed and peer
30 reviewed.

Results: During treatment, a prostate position offset of nearly 3 mm in the posterior direction was
observed with KIM. This position offset did not trigger a gating event. After the treatment, the
35 prostate motion was independently measured using kV/MV triangulation, resulting in a mean
difference of less than 0.6 mm and standard deviation of less than 0.6 mm in each direction. The
accuracy of the marker segmentation was visually assessed during and after treatment and found to be
performing well. During treatment there were no interruptions due to performance of the KIM
software.

Conclusions: For the first time, KIM has been used for real-time image guidance during cancer
40 radiotherapy. The measured accuracy and precision were both sub-millimeter for the first treatment
fraction. This clinical translational research milestone paves the way for the broad implementation of
real-time image guidance to facilitate the detection and correction of geometric and dosimetric errors,
and resultant improved clinical outcomes, in cancer radiotherapy.

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INTRODUCTION

50 Tumors in the thorax, abdomen and pelvis move during cancer radiotherapy. Many methods have been developed to measure the position of the tumor in real-time including kilovoltage, megavoltage, and kilovoltage/megavoltage/respiratory sensor combinations, magnetic resonance imaging, and ultrasound. Three implanted marker-based methods that have been applied clinically are stereoscopic kilovoltage x-ray,¹⁻³ electromagnetic⁴ and radioisotope tracking.⁵ These methods all rely on hardware that is additional to a modern linear accelerator. In this work, we describe the first clinical implementation of kilovoltage intrafraction monitoring (KIM), a method that uses a gantry-mounted
55 kilovoltage x-ray imager to determine the real-time 3D position of implanted markers during cancer radiotherapy.

METHODS

60 The KIM method, hardware, software and clinical process are briefly described. All necessary ethics, legal and regulatory requirements were met. The legal processes included agreements between the clinical site, the Royal North Shore Hospital and the additional parties providing software or hardware, including the University of Sydney, Aarhus University and Varian Medical Systems. The regulatory pathway included filing a Clinical Trial Notification with the Australian Therapeutic Goods Administration.

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KIM method

The heart of the KIM method is the 2D to 3D transformation first described by Poulsen in 2008⁶ and extended in 2009.⁷ This transformation relies on the correlation of motion between the observed and unobserved directions. The motion in the unobserved direction is estimated based on the correlation of motion computed using prior observations from angles where the currently unobserved direction was observed. A probability density function (pdf) of the correlations is determined via maximum likelihood. The pdf, recomputed after each new image, is used to estimate the position of the markers in the unobserved direction, yielding the 3D target position.

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75 Another key element of KIM is the robust automated marker detection algorithm⁸ where the marker shape is known *a priori* and the pose of each marker is determined during a short pre-treatment arc.

KIM hardware

80 KIM requires a gantry mounted x-ray imager in which the images can be acquired during treatment and the images and gantry angles can be immediately accessed. In principal, this requirement covers linear accelerators from Elekta, Varian and other manufacturers. The current implementation used a Varian (Palo Alto, CA) Trilogy linear accelerator with an On Board Imager. The images were streamed via a frame grabber cable to the iTools Capture software (Varian) on a stand-alone research computer on which the KIM software was also installed. Though relatively minor, this additional
85 hardware would not be necessary in a vendor implementation of KIM as the images are directly streamed to the treatment console. In our set-up, there was no connection between the KIM software and the treatment console, and therefore additional safety checks were necessary, and the beam pause and couch correction when motion exceeding the gating threshold was observed is manually performed.

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KIM software

The KIM software is an in-house written a C# application running in the .net environment. The interface was developed with substantial radiation therapist input to maximize key information display and screen space. Examples of the interface are shown in Figure 1. The clinically-used
95 version of the KIM software was branched from the ongoing research version, with changes, bug tracking and feature requests under version control. Algorithm parameters include the number of images used to build the pdf (when more than 500 images are acquired, the oldest images are discarded), three-image frame averaging and the automatic switch to a joint template if the markers overlap.⁹ The latency of the KIM hardware/software was measured to be less than 350 ms.¹⁰

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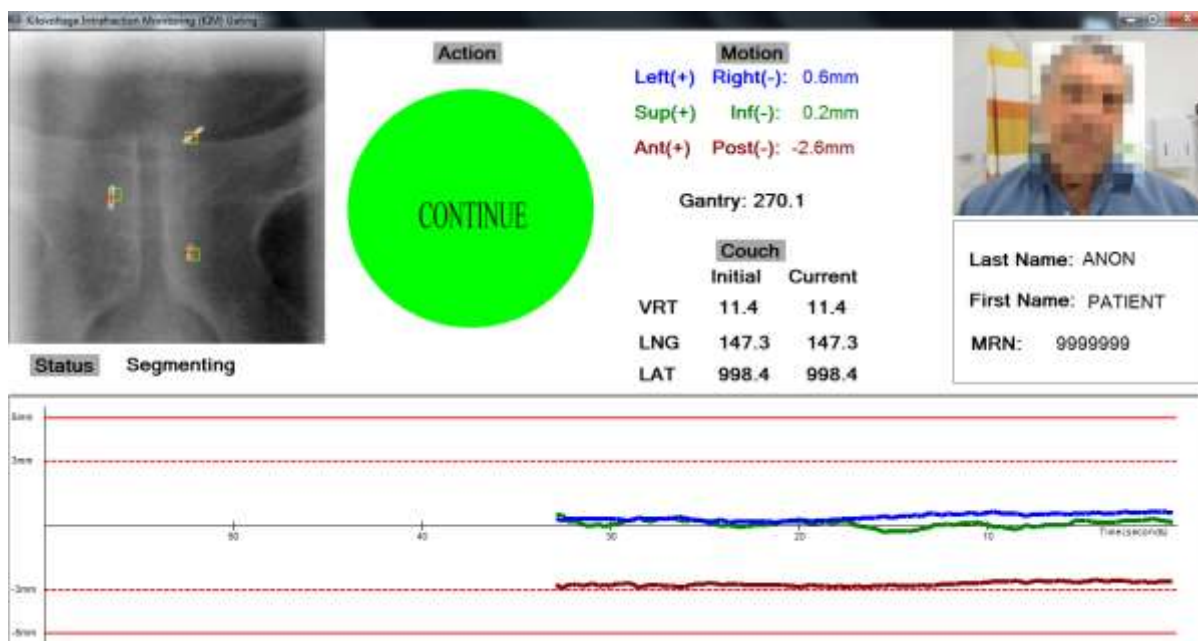


Figure 1. The KIM user interface. Key features include *Top Left*: the real-time prostate image showing the detected marker positions in the image (red crosses) and also the marker positions from the treatment plan in the same projection image (green squares); *Middle*: the therapist action directive (continue, warning, stop treatment); *Top Right*: the patient picture and medical record number for patient safety purposes and *Bottom*: the measured motion trace in each dimension.

Clinical process

The patient was treated as per the clinical trial protocol (NCT017424030). During treatment planning, to avoid manual entry of offsets at treatment delivery, the treatment isocenter is set to the center of the three markers. Through an Eclipse script, the individual marker positions, patient name and medical record number (MRN) are written to a file. This file along with the patient picture is put into a folder on the KIM treatment computer. Prior to treatment, the file and patient picture are read into the KIM software. For safety, the patient name, MRN and picture are compared to that on the treatment console as currently there is no communication between the KIM computer and the treatment console. The marker positions are used to define the initial search region for the marker detection software, and used throughout treatment for safety as the detected marker positions and the marker arrangement should be close to that from the original CT scan. The current couch position is manually entered to guide fast correction in the case of a gating event.

Prior to treatment, a 120-degree pre-treatment kV arc is acquired to build the KIM pdf. After a 3-4 second delay, treatment is initiated with continuous kV imaging during which the images are processed and the 3D prostate position is determined. KIM during treatment is a real-time implementation of a previously published offline KIM clinical study,¹¹ with Figure 3 of that paper showing the workflow. The clinical protocol gating parameters for the study requires the treatment to be paused if the target moves 3 mm or more from the planned position for 5 seconds or more. In the current implementation of KIM, the beam pause or gating event is manually performed by the radiation therapist.

The kV image acquisition was the same as a previous offline KIM prostate study.¹¹ Briefly, the images were acquired at 10 Hz with exposure parameters 125 kVp, 80 mA and 13 ms. The field size was $6 \times 6 \text{ cm}^2$. To reduce the effects of the MV scatter on the kV images the source-detector distance was 180 cm. With these parameters over a 39-fraction treatment the physical dose is estimated to be 1.2 Gy,¹² with an effective dose of 50 mSv.¹³ The increased imaging dose is a disadvantage of KIM, however there are a number of strategies to substantially reduce the imaging dose, several are which are described in Ng *et al.*¹¹

Patient treatment details

140 The patient for the trial had localized stage T2a prostate cancer with PSA 7 nG/mL and a Gleason
score of 7. He is being treated to 80 Gy in 40 fractions using dual arc RapidArc and has three
implanted gold markers of diameter 1.2 mm and length 3 mm. To account for contouring variability
and other uncertainties in the radiotherapy process, his CTV to PTV margins were 7 mm in all
directions except posteriorly where the margin was 5 mm. The first patient to be treated with KIM is
shown in **Error! Reference source not found.**

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Figure 2. The first KIM patient in treatment position.

KIM quality assurance

150 The quality assurance (QA) process was adapted for KIM target position monitoring from that used
for real-time electromagnetic monitoring by Santanam *et al.*¹⁴ The KIM QA process is described in
more detail in Ng *et al.*¹⁰

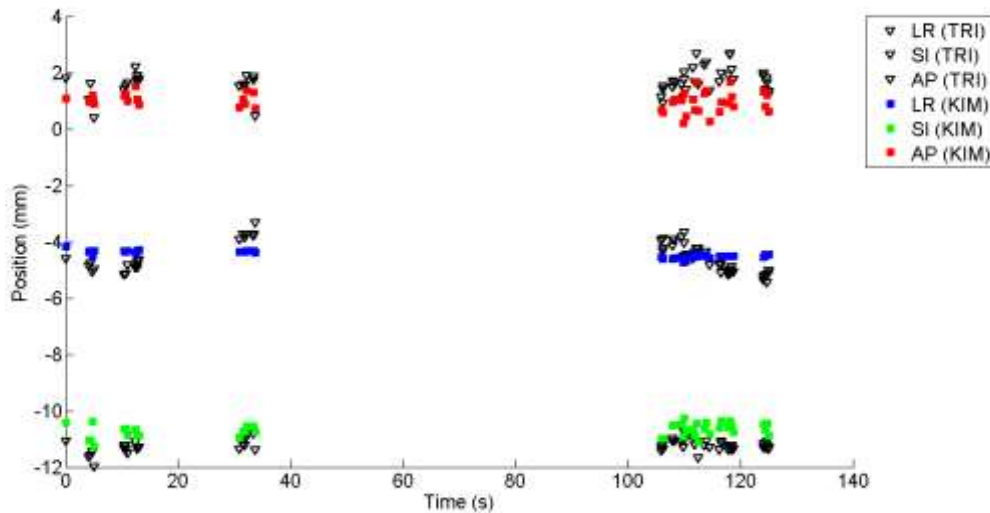
RESULTS AND DISCUSSION

155 The total treatment time for the fraction, from walking into the bunker to exiting the bunker, was 26
minutes. This time included CBCT imaging and all of the typical first fraction checks. As the KIM
software is not integrated with the other treatment software, there are some process inefficiencies and
additional checks implemented which increase the total treatment time.

160 The pre-treatment arc, and two treatments were completed with the kV images being streamed to the
KIM software and processed as shown in Figure 1. During treatment, a prostate position offset of
nearly 3 mm in the posterior direction was observed with KIM, however this positional offset did not
exceed the 3 mm for 5 seconds action threshold. An anonymized movie of the treatment is attached
as supplemental material. To quantify the accuracy of the KIM method, kV/MV triangulation^{11, 13} was
165 performed where the markers were within the treatment field and clearly apparent on an MV image
the cine acquisition. Fiducial marker positions measured retrospectively by kV/MV triangulation and

the corresponding fiducial marker positions estimated in real-time by KIM are shown in Figure 3, along with the direct position measurements determined from kV/MV triangulation.^{11, 15} Averaged over all of the markers and images where the markers were clearly apparent the mean difference between the retrospective triangulation and real-time KIM were, in mm, LR 0.22, SI 0.56 and AP -0.07. The standard deviation of the difference was, in mm, LR 0.57, SI 0.27 and AP 0.32.

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Figure 3. Fiducial marker positions measured retrospectively by kV/MV triangulation (triangles) and the corresponding fiducial marker positions estimated in real-time by KIM (squares).

From the measured motion, dose reconstruction was performed using the method of Poulsen.¹⁶ The planned and delivered isodose distributions and dose volume histogram curves are shown in Figure 4 and Figure 5 respectively. It should be noted that the current clinical version of KIM, and the dose reconstruction method, do not measure or account for rotation or deformation that will have an impact on the actual dose delivered to the patient. Even though the gating threshold was not exceeded for this fraction, there was benefit to KIM in the ability to estimate the delivered dose, including motion, which is not possible without KIM on a standard linac. Furthermore, had KIM been integrated with MLC or couch adaptation, which we plan to do in the future, an improvement in the agreement between the planned and delivered doses would have been possible.¹⁷

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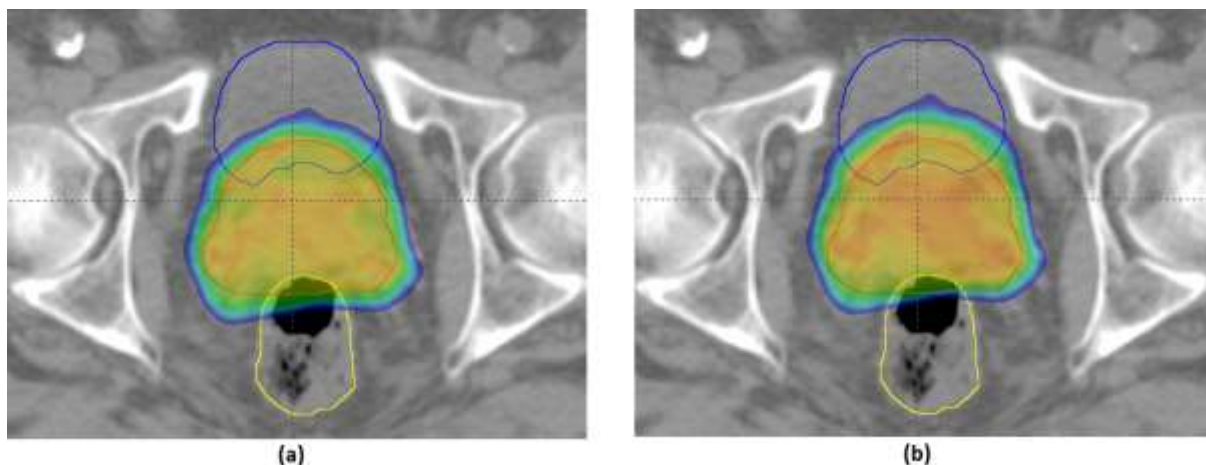


Figure 4. (a) Planned isodose distributions and (b) estimated delivered isodose distributions based on the KIM-measured motion trace for fraction 1 of patient 1. Dose levels >80% are shown. Contoured are the bladder (blue), PTV (red) and rectum (yellow).

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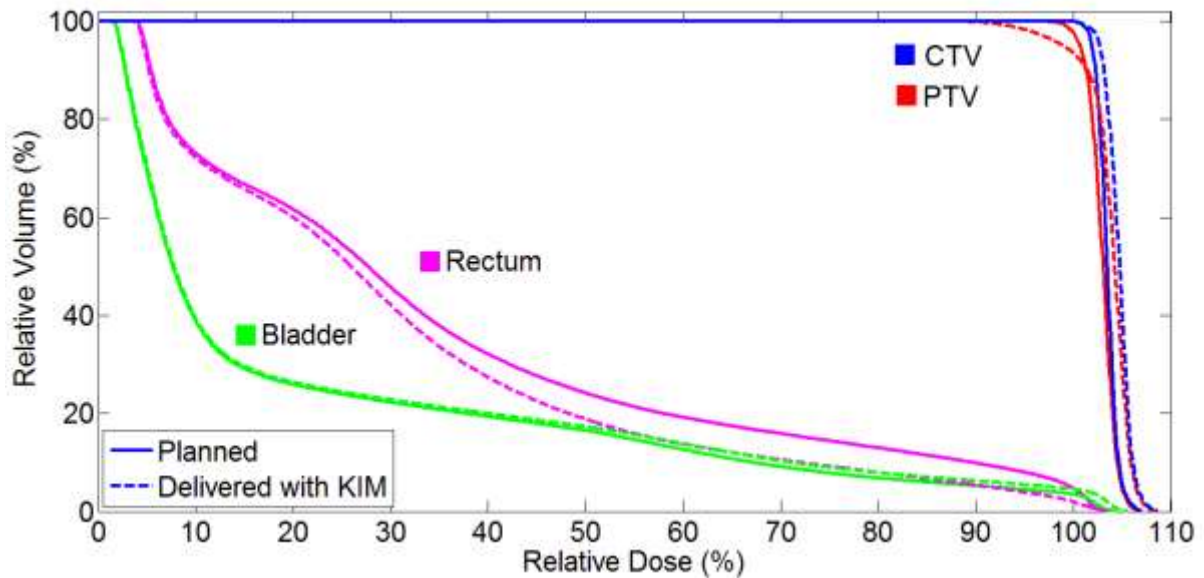


Figure 5. Planned (solid lines) and estimated delivered dose volume histograms (dashed lines) based on the KIM-measured motion trace with KIM for fraction 1 of patient 1.

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Future directions for the clinical implementation of the KIM method include extending to more prostate patients, SBRT, other cancer sites in the thorax, abdomen and pelvis, rotation, and potentially deformation. Additionally, imaging dose reduction methods could be explored as well as the integration with a respiratory monitor for cancer sites affected by periodic motion.

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This clinical implementation of KIM was performed on a Trilogy linear accelerator. As the KIM method requires only a gantry-mounted x-ray imager, the method could be applied on other linac models from the same vendor or linacs from other vendors provided the terms of the KIM technology (US Patent 8,379,794) Stanford University license are adhered to.

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Currently, the response to above tolerance motion by KIM is manual gating. Obvious next steps to improve safety and efficiently are to make this gating process automated and/or to link KIM to automatic MLC or couch adaptation.

CONCLUSION

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After eight years of research and development, for the first time KIM has been clinically implemented for prostate cancer radiotherapy. The measured accuracy and precision were both sub-millimeter for the first treatment fraction. KIM is a real-time image guidance method using widely available radiotherapy technology. This clinical translational research milestone paves the way for the broad implementation of real-time tumor position monitoring with the detection and correction of geometric and dosimetric errors and resultant clinical outcomes in cancer radiotherapy.

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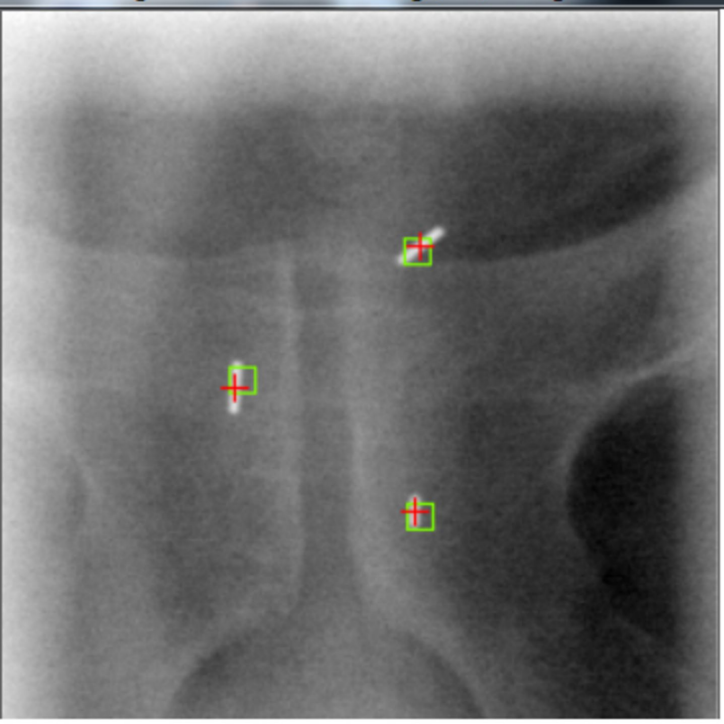
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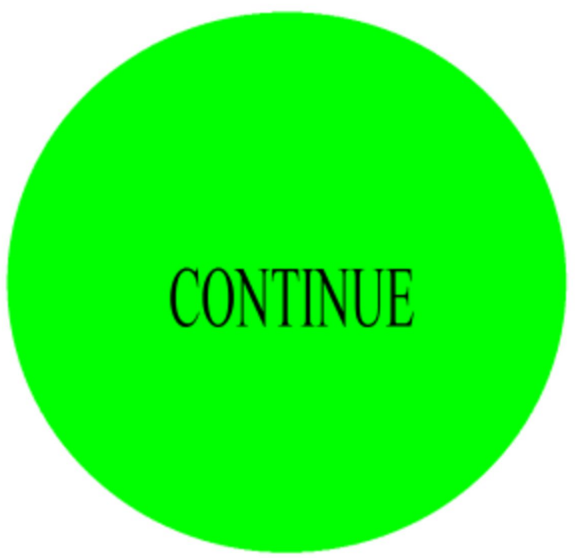
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Status Segmenting

Action



Motion

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Sup(+) Inf(-): 0.2mm
Ant(+) Post(-): -2.6mm

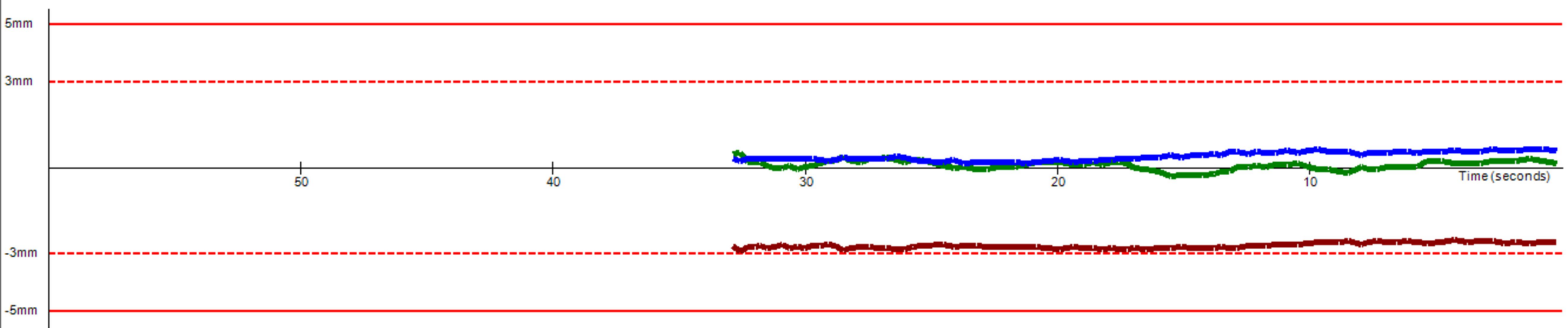
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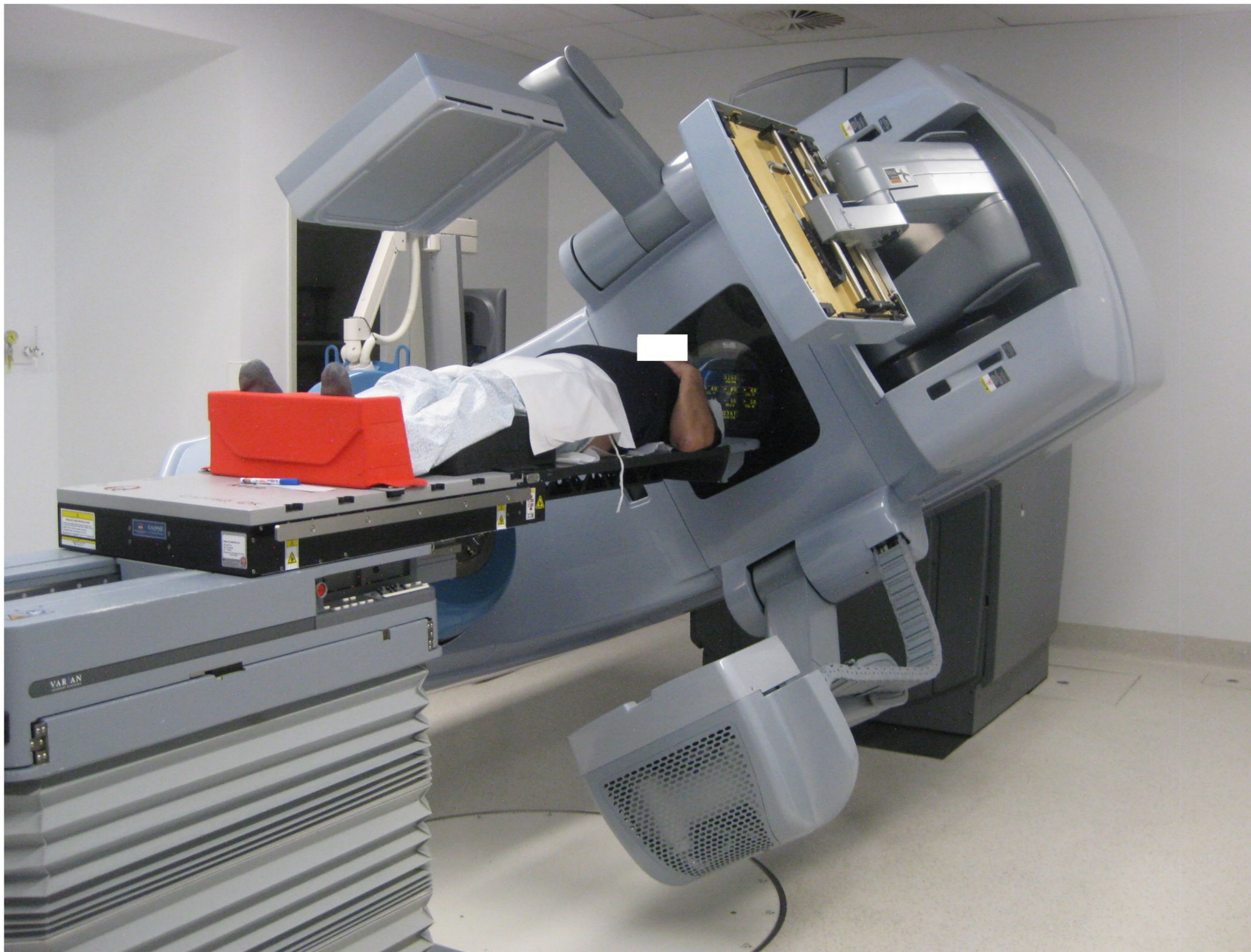
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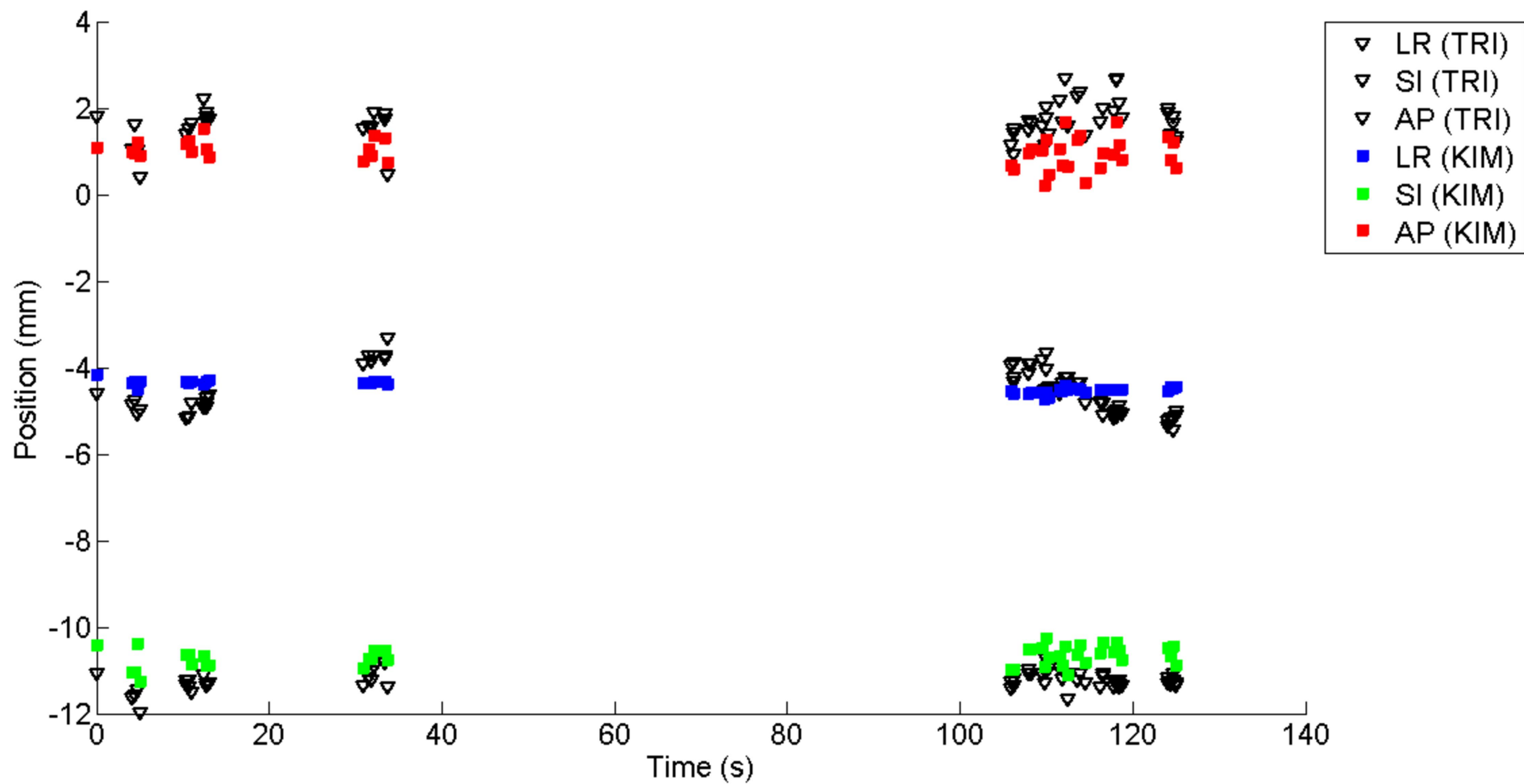
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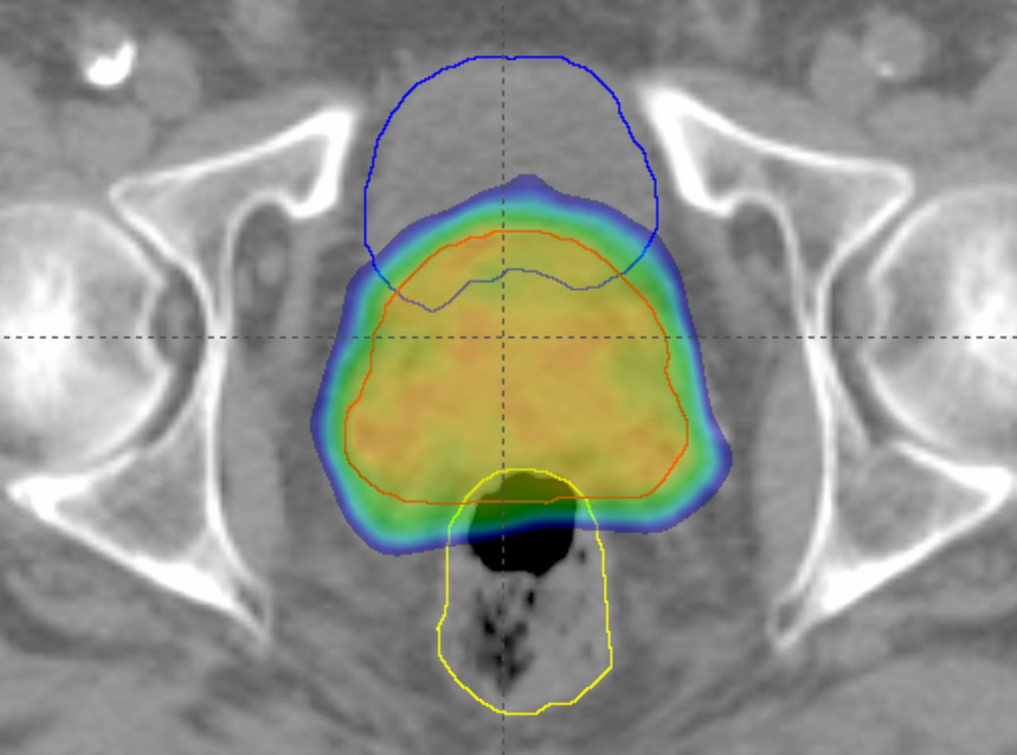


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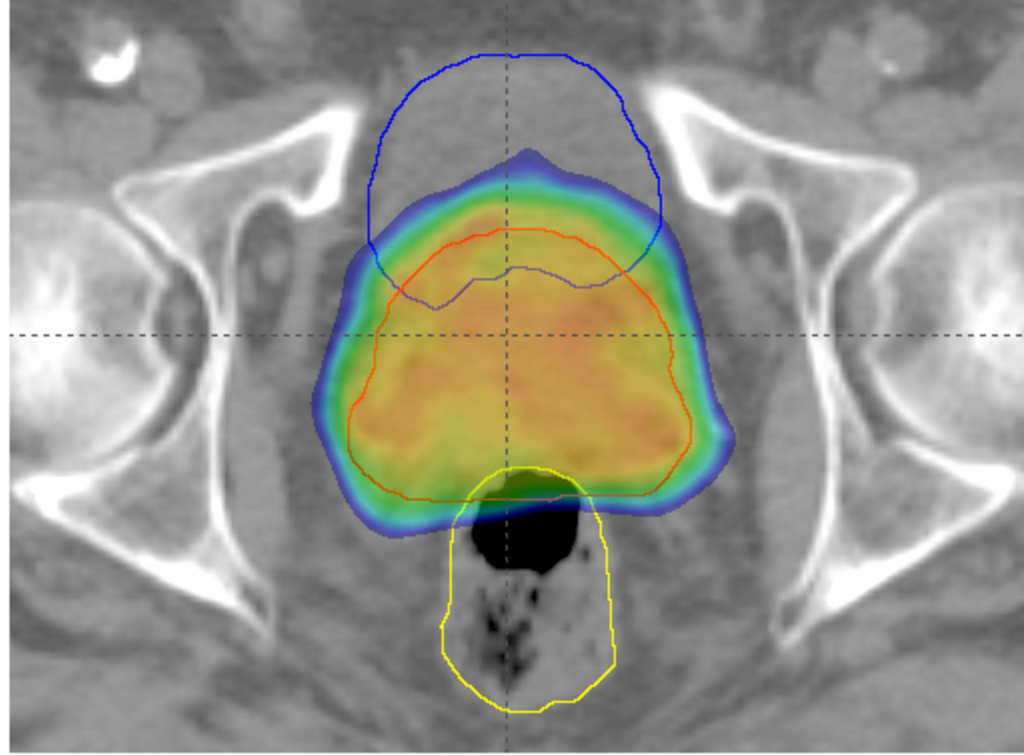








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(b)

