SYNCHRONY® ON THE RADIXACT® SYSTEM

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Radixact®

ABSTRACT

The Radixact® system from Accuray now has Synchrony®, real-time motion synchronization technology, and clinics are using it to treat patients without any ITV (Internal Target Volume) and with no gating. This is the only automated tumor tracking and live beam steering helical radiotherapy system currently available on the market as of September 2021. Synchrony is distinct from other motion management or compensation methods and all current forms of beam gating because of sophisticated predictive modeling of the target position that brings the beam steering in synch with the target motion. The delivery is therefore implicitly correcting for latency at all times during a respiratory treatment fraction. It brings motion blurring down the order of a millimeter or less with 100% passing rates for a bank of 3%/3 mm respiratory dosimetry tests. The system is fully automated with user robustness and intervention control, described herein. Radixact Synchrony was developed and trained on a full range of realism: from realistic anthropomorphic phantoms that span reasonable anatomical size ranges, to simplistic ones used for quality assurance that are cross-validated with the former. Both realistic and common regular motions as well as a variety of motion stages and actuators were used in development. Quality assurance procedures were developed out of this process and are described.

OUTLINE

I. THE SYNCHRONY® APPROACH

It is true that we are at a tipping point with motion management in radiotherapy (*Keall et al., 2018*), and this paper describes another truth – Accuray is already there. The current common clinical practice in radiotherapy is to account for organ and tumor motion with the addition of a significant Internal Target Volume (ITV) margin: respiratory motion for lung tumors as a common example (*Keall et al., 2006*). With Synchrony, the motion blur is reduced so far as to be functionally eliminated for many cases. One can expect the residual blur for a typical Synchrony respiratory treatment to be on the order of the slice thickness or less of the planning Computed Tomography scan (CT) and for setup errors to be eliminated. A residual blur this small might require a new discussion about margins, with motion no longer dominating the total margin size calculation.

Accuray Synchrony nearly eliminates respiratory motion dose errors by actively tracking the target and then steering the beam at the same strength to a modeled position a small bit ahead of time (respiratory motion mode). System latency does indeed matter for beam steering at respiration motion rates – the tracking can easily be off by a millimeter without a model, no matter how good everything else is. The modeled position is the result of sophisticated software that adapts in real time: fitting and so anticipating the found positions and their timing. Synchrony therefore goes beyond just tracking the target motion for its respiratory modes; it implicitly uses this small prediction time to automatically steer and widen (dwell, scatter, etc.) the beam just right to retain the planned dose. The beam is therefore in position for the correct dose rate when the target is there too, in synch (in respiratory modes). The precise physics terminology is that Synchrony literally synchronizes the dose rate per voxel with adaptive beam steering for all times during the treatment, leaving only a small residual blur related to spatial resolution and geometric constraints. Because the modulation of dose rate itself is being synchronized, interplay effects *(Bortfeld et al., 2002)* are eliminated as well as most blurring. The whole process is automated and made robust with a variety of user diagnostics on the tracking, the motion modelling, and the beam steering, with the ability to pause and intervene instantly as desired. For many treatments, one can build a model, judge it as good, then deliver a fully automatic treatment with little or no intervention. A correlation is formed between a sophisticated respiratory model, sequential x-ray snapshots of the patient's interior, and continuously streaming LED marker positions on the patient's surface for high time resolution. The movement of the LED markers is followed with a model that updates with x-ray snapshots. All the randomness is followed exactly, even through coughs, as long as the correlation is retained between physiology at depth in the patient and the physiology on the surface of the patient.

This paper will very briefly describe some physics behind Synchrony delivery, its robustness in the hands of a user, and also will summarize the performance assessments that were done including the phantoms used in those assessments. This paper will also present some quality assurance choices, example test round performance results showing sub-millimeter RMS tracking errors and 100% passing rates for dosimetry tests. Then, finally some early example clinical results from a collaborating clinic showing the gains achieved with reduced margins using Radixact Synchrony®. They have, in general, decreased their PTV size by about 30% allowing for a boosted tumor dose.

1.1 Synchrony from CyberKnife® to Radixact®

The first helical TomoTherapy® (HT) *(Mackie et al., 1993)* System is developed by Accuray Incorporated (Sunnyvale, CA USA). This device has been upgraded to Radixact® 2.0 with Synchrony® and is also currently in clinical use (Chen et al., 2020). Yet, Synchrony has actually been in clinical use for CyberKnife® Systems for many years, and it has been well characterized (Nuyttens and van der Pol, 2012 for example). As opposed to CyberKnife that has two orthogonal kilovoltage X-ray tubes far from the patient (Seppenwoolde et al., 2007), the Radixact System has an entirely different geometry. The CyberKnife robot has the obvious advantage of being able to steer the beam source and its collimation together from any angle to any position. The Radixact version must accomplish an equal off-axis dose rate with no steering or changes in the beam source position, but by steering the beam only from collimation changes alone: the jaws (each edge separately) and the binary multileaf collimator (MLC). One notable advantage Radixact has is the ability to add or change the imaging angles at any time live during treatment such that large bony obstructions are therefore easy to avoid when tracking.

2. ALGORITHM OVERVIEW

Recall that the treatment goal is fundamentally just the accumulation of dose to each voxel x,y,z of the tumor (and critical organs) matching the planned dose, D, in the target, as prescribed. A simple mathematical description of this process is as follows: the dose, D, at x,y,z equals the sum of all the beams, D, over time, t, even as they move, x'(t), y'(t), z'(t):

$$D(x,y,z) = \int_0^{T\_Fx} \dot{D}(x - x'(t), y - y'(t), z - z'(t), t)dt \ . \quad (1)$$

Here, the quantity representing the beam, D, is the dose rate for a voxel (ignoring latency for now) within the treatment time for a fraction: from 0 to T_Fx.

The following are ways to manage this motion of the beam position relative to the target position:

1. **Maximize Use of the Integral (Optimized Margins and Reducing Interplay):** Optimized Margins and Reducing Interplay: If not using active motion management or compensation of any kind, one can still use the treatment schedule statistics with assumptions with averaging from the integral in Eq. 1 to find an optimal margin size *(Ecclestone et al., 2013)*. This also eliminates the ITV (by name anyway), but there is still a motion margin that is significant.

   Motion induced nonuniformity (interplay with beam modulation) can also be effectively averaged away *(Bortfeld et al., 2002)*. For HT and therefore Radixact®, respiratory treatments are naturally robust to interplay, except for lower frequency drifting *(Kissick et al., 2008, Kissick et al., 2010)*. Margin discussions already often left out interplay *(Kissick and Mackie 2009)*, but now, these passive approaches to motion are becoming obsolete and contra-indicated with hypofractionated dose schedules. Treatments now require intrafraction motion management and compensation.

2. **Gating:** Instead of the integral limits in Eq. 1, gating chops out pieces in time when image guidance indicates x-x'(t),y-y^'(t),z-z'(t) are minimized to a certain predetermined level. However, the beam itself remains unchanged. The change to Eq. 1 is just in the limits as follows:

   $$0 \text{ to } T\_Fx \quad \rightarrow \quad T_{gate1start} to\ T_{gate1end},\ T_{gate2start} to\ T_{gate2end}, \ldots \quad (2)$$

   One is still left with the sum of many smaller integrals, each representing blur and interplay that do not go away, and with a tradeoff to overall treatment time. In addition, one is often not using a predictive model: those systems assume the position now is the last observed one.

3. **Synchronization:** This method involves modeling, and both tumor tracking and beam steering, and widening. The model implicitly includes prediction, since it adjusts for the closest match at all times. It minimizes motion margins the most. It eliminates registration errors and drifting errors to the level of the planning CT resolution. Referring to Eq. 1, it does the following:

   $$\dot{D}(x - x'(t), y - y'(t), z - z'(t), t) \quad \rightarrow \quad \dot{D}(x, y, z, t)\ , \quad (3)$$

   within geometric constraints. The relative motion and any change in beam strength is minimized for every time for the whole fraction. In effect, this gets inside Eq. 1 to the integrand level. Ideally, every voxel would experience no relative motion to the beam, but resolution limits and geometric constraints mean it is less than perfect at doing this of course.

Synchrony® for Radixact® is rather robust to planning technique and to planning CT quality. A wide range of CT scan conditions and doses were used on the same anthropomorphic setup with only mild effects on the tracking behavior. The software filtering of the images makes it robust.

2.1 New Hardware and the Geometry

The Radixact® System accomplishes the third method above with innovative new software and with new hardware. The ring gantry of Radixact now contains both the x-ray tube and the flat panel detector mounted on the gantry, much closer to the patient with more scatter radiation in the image than CyberKnife®. For more details about the new hardware and kV doses, see Schnarr et al., 2018 and Chen et al., 2020. Also added are a camera and LED (Light Emitting Diode) markers for respiratory treatments needing the high time resolution.

The most obvious imaging difference for active tracking is the fact that Radixact must weave together successive monoscopic views from the flat panel detector to arrive at a 3D position of the object being tracked (*Schnarr et al., 2018*). See Figure 1 for a simple overview of the geometry of the Radixact device.

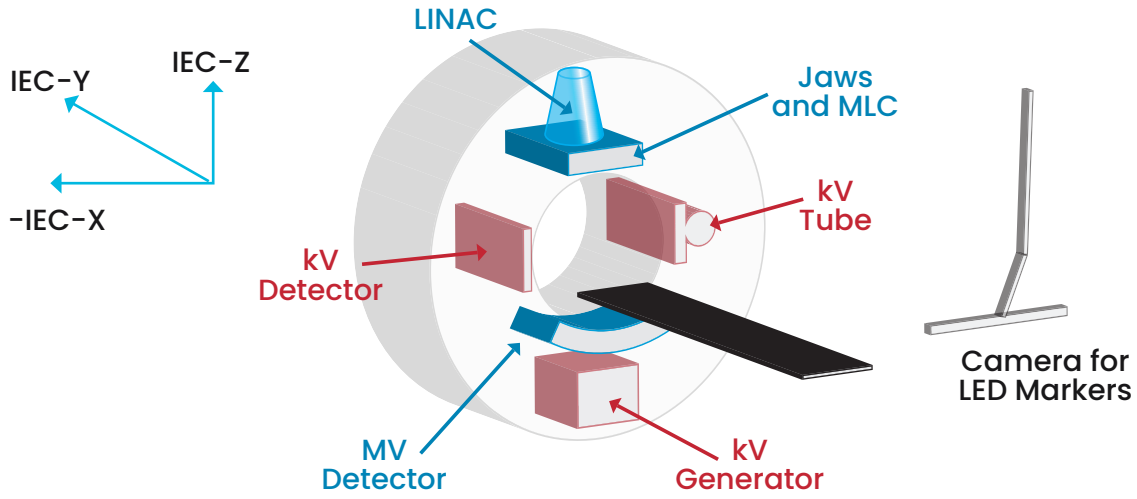

Figure 1: *Radixact gantry geometry. Note that the couch goes into the bore during treatment. The LED camera is shown on the right side hanging from the ceiling (adapted from:* ***Schnarr et al., 2018****).*

The Radixact System has two principal ways to shift the beam: collimation into and out of the bore is controlled by the jaws (IEC-Yf coordinates), and axially, perpendicular to the couch motion, with a binary MLC that modulates the beam in IEC-Xf and IEC-Zf. The relative dynamics are of note: the movement through the jaws includes many breathing cycles, but many leaf movements occur for each breathing cycle. Interplay errors for helical TomoTherapy® are therefore naturally minimized by this wide separation of frequencies (*Kissick et al., 2008*).

2.2 Synchronization Modes
The motion synchronization system tracks gold fiducials or lung tumors by using an on-board kilovoltage (kV) x-ray system to obtain live positional target offsets, and LED markers on the patient surface to achieve high time resolution between kV snapshots for respiratory modes. A correlation model then continuously self-updates to construct a live modeled target position throughout treatment.

There are three modes of motion synchronization for Radixact® as follows:

1. Synchrony® Fiducial Tracking™: tracks gold fiducials without predictive modeling.
2. Synchrony Fiducial Tracking with Respiratory Modeling: tracks gold fiducials that exhibit respiratory motion, in the lung or in other nearby organs.
3. Synchrony Lung Tracking with Respiratory Modeling: tracks a lung tumor that exhibits respiratory motion, without needing any implanted fiducials.

The non-respiratory mode of option 1 has no predictive model and so it will exhibit a lag or latency in its response to a position jump, a worse lag if the jump is all within the axial plane. Recall that each snapshot gives a mixture of IEC-X and IEC-Z, and it will require 2 snapshots to get both x and z. Jumps in only IEC-Y will lag half as bad. Respiratory modes overcome this lag with a predictive respiratory model. The process is fully automated while still allowing for user intervention.

2.3 Algorithmic Spatial Behavior
The 3D position is calculated by interpolating across successive monoscopic images. The advantage for the Radixact System is that any angle is possible. The Radixact X-ray tube (only one) does allow for every possible axial angle, and they can be changed during treatment. That view flexibility is a significant advantage. It enables one to avoid large bony obstructions for example. Before the 3D position of the object is calculated, a 2D position on the flat panel detector at a given angle must be calculated. Dose itself is not recalculated live for patient deformation, as the speed for that level of live calculation is still far into the future for the whole field. Fortunately, deformation effects, though small, would tend to average away for Radixact just as interplay effects would do (Kissick et al., 2008).

2.3.1 Object Recognition
One type of trackable object is a cluster of fiducials (many standard sizes work) but they need to have the density of gold to work well. The algorithm finds the location of an object by maximizing the cross-correlation between two 2D images: a filtered DRR (Digitally Rendered Radiograph) of the planning CT taken through a specified angle, and a recently acquired kV snapshot from the newly added Radixact hardware, also filtered, and also from that same angle. The object recognition algorithms are designed to work for both patients and standard phantoms used in quality assurance and quality control (QA).

A fiducial is located on the image using information of both its edge shape and contrast and its overall density too. The algorithm attempts to select out just the object of interest from the CT in an effort to avoid other external geometries, and the filtering of the images is optimized from previously obtained and anonymized patient images, and phantom images too, and with a variety of gold fiducals. With more than one fiducial, it also calculates the cluster centroid. The user can control the tolerance the system will allow for the fiducial cluster deformation (“Rigid Body” parameter).

A non-fiducial object (lung tumor) with sufficient edge recognition is tracked – the centroid is calculated in 2D first, just as the centroid for the fiducial case was first calculated in 2D. The object that has unique edge gradients and shapes for each direction tends to match better than say a simple sphere that has the same small edge from every view. Care was therefore taken during development to make sure that the algorithm also worked for simplistic shapes often found in QA phantoms.

2.4 Algorithmic Temporal Behavior

When treating using thr Radixact® System with Synchrony®, the user now 'drives' a dynamic system. The Treatment Delivery Console (TDC) provides real time information and the ability to change and adapt treatment as it happens. It is automated, but the user can intervene at any time in a variety of ways. The user learns when and how to intervene and when to let it cruise well.

For the non-respiratory mode, the model is just a 3D position calculation and it is updated every snapshot. Note that it will require two successive kV snapshots to fix the position of the target, plus about 1.5 seconds of processing time. One can then set an autopause delay time: the time for a pause of the beam if the target position is not found with a high enough level of confidence.

For respiratory modes, a model implicitly predicts the motion into a short time ahead to overcome latency. A mathematical model of either the fiducial constellation or the tumor outline is used to construct the offsets to quickly re-point the beam. The overall remaining latency in the respiratory motion synchronization system is of the order of +/- 10 ms.

The surface movements of the patient are tied to the internal tumor motion with a updating live correlation. This correlation model is used for respiratory motion only. It ties the LED marker data from a camera above the foot of the couch (see Figure 1) to the tumor motion sampled with the kV snapshots. Both a simple 1D model and a more sophisticated 5D model are used for this correlation (Low et al., 2005, Zhao et al., 2009 but upgraded to use velocity instead of tidal volume: Schnarr et al., 2018). The model updates by minimizing the difference between projections of the measured positions and the modeled positions by adjusting model parameters and amplitudes in each direction at each snapshot time.

The system has ways to make this modeling process robust for respiratory modes. It keeps a spare model in the background in case the original one no longer is good to use to save time developing a new model with a new set of images (see Figure 2). The design is that it builds a good model up front and uses it, all the while calculating a replacement model in the background. If the new one is out of correlation, the most recently calculated one is used. This process reduces errors and hones delivery into a good stable model that only disrupts when various indicators reach set points or limits. The next major section describes user control further.

In addition, the system keeps track of the model age. Since it tries not to keep resetting the model if it was good to start with, it will keep using it up to a certain point the user feels would be safe. If the user thinks they have calculated a very good model, they can set the delay such that it will use that model for the whole treatment. The user could also set it to always update every kV snapshot if desired.

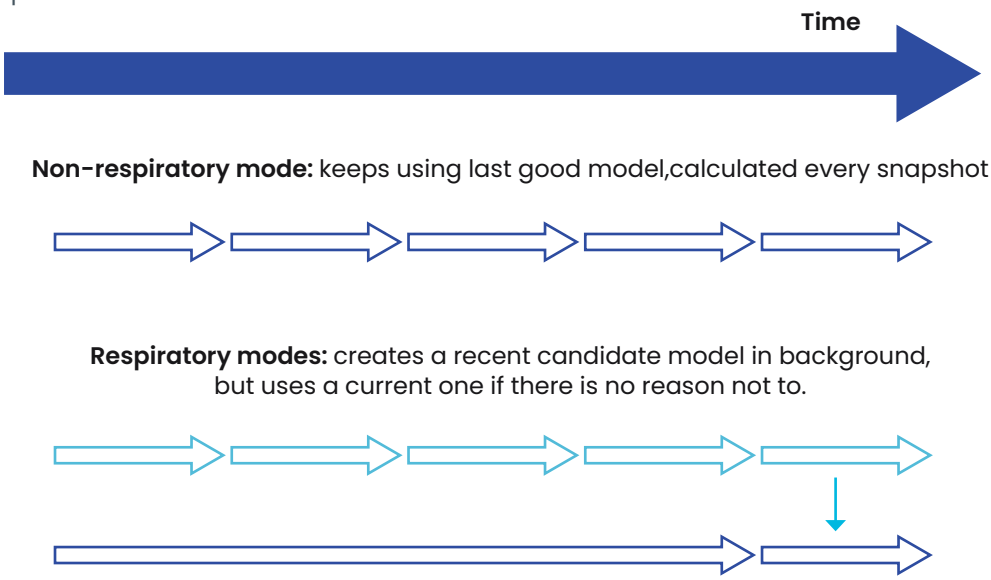

Figure 2: *An illustration of the Radixact® Synchrony® model building behavior in time for two types of modes: respiratory and non-respiratory. Note that respiratory modes keep a spare, most recently, calculated model in the background.*

A form of aliasing can occur for respiratory treatments with regular motions. It is not the same concept as traditional aliasing in that the frequency cannot be incorrect. In this case, the aliasing takes the form of insufficient coverage of the breathing cycle by the kV snapshots. If significant portions of the breathing cycle do not have kV snapshots the can be too little information to sufficiently constrain the model. The TDC has mechanisms to show the user the breathing phase coverage, allowing the user to monitor for the possible occurrence of aliasing. It is worth noting that extremely regular breathing is required for the effect to be significant. Internal investigation of the effect with real patient data determined that only a few percent of patients could breathe regularly enough for this to be a problem; in general, normal patient breathing has sufficient natural randomness to drive building good models. The warning regarding this effect extends mainly to physicists who might encounter the effect while using a purely regular waveform for QA or other investigations.

2.5 Dynamic Control and Robustness

The correlation model of the respiratory modes is continuously adapting and updating. The user controls how old that model can become and when to replace it. The system is automated, and many treatments need little or no user intervention. The system can also be 'driven manually' with the user able to pause and rebuild the model at any time desired. The user has many diagnostics on the TDC to diagnose the model uncertainty the tracking fidelity.

The following quantities are the major ones to help the user correctly deliver this dynamic treatment:

Potential Difference: This quantity gives the overall model uncertainty. It is continuously updating and is plotted for the user. Since the tracking error will vary depending on the motion itself, the error is in general ellipsoid about the modeled position and not a sphere. Potential Difference is defined as the major radius of that uncertainty ellipse: it includes rrors from all sources to the model. See Figure 3 for an artistic vision of how one might the conceive of it in relation to other spatial quantities.

- Measured Delta: This quantity is the 2D error in finding the object at each kV snapshot. It is measured at the object plane thereby removing what would be an oscillating magnification effect for the quantity if it were left at the image plane. See Figure 3.

- Rigid Body: This quantity is also a 2D error, but this one is related to fiducial arrangement changes. It is measured at the object plane as well for similar reasons. See Figure 3.

- The user has control over thresholds for these quantities. After some experience, one learns to contrast information between these quantities to pin down any behavior that could be a concern. The system will autopause for a variety of reasons. In addition to exceeding limits that the user sets, it will also interrupt the beam if the model age exceeds a preset limit.

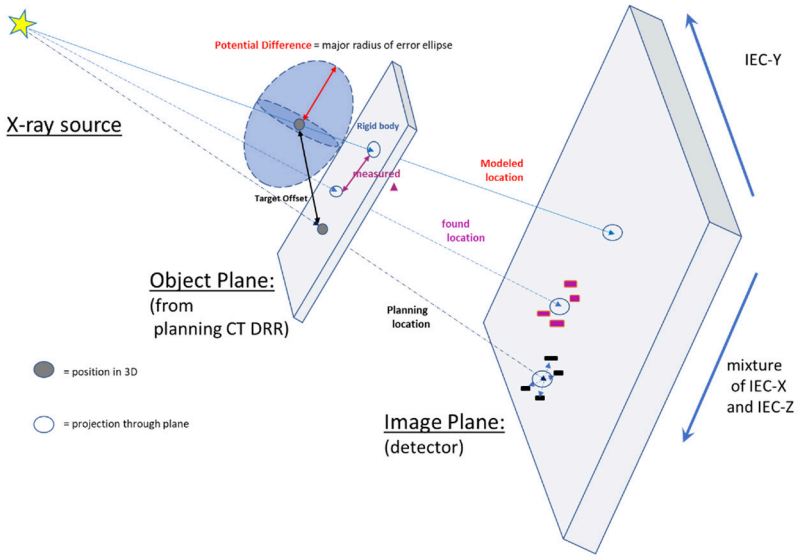

Figure 3: *Schematic representation of the spatial relationships for Radixact® Synchrony® (not to scale). The beam is delivered to the modeled position. Potential Difference describes the 3D uncertainty of that position. Measured Delta describes the error associated with finding the object in 2D with magnification effects removed. Target offset describes the 3D change in position from the plan. Rigid Body describes the distortions in the arrangement of the fiducials in 2D at the object plane.*

3. PRODUCT DEVELOPMENT SYSTEM TESTING

Key system testing focused on tracking fidelity and its manifestations in the dose distribution of a Synchrony® delivery. Fundamental to the tracking success was the object recognition in 2D. It was important for the design of the product to include robust tracking and modeling on both QA phantoms and real patients. To that end, the system was tested and tuned using a variety of phantom types and configurations. Additionally, throughout development, we used a wide spectrum of tumor motions ranging from regular sinusoids to hundreds of real patient traces sampled from both prostate motion and lung tumor motion.

3.1 Phantom Systems

A suite of phantoms was constructed and assembled to develop and test both the tracking behavior and also the dosimetric behavior. The phantoms for development described are similar and are compared to some others on the market in *(DeWerd and Kissick, Ed., Springer, New York, NY, 2013)*. To the best extent possible within reason, the phantoms also moved realistically, with motion displacement probability distributions typical *(Huang et al., 2015)* of real prostates *(Kitamura et al., 2002, Willoughby et al., 2006)* and real lung tumors *(Seppenwoolde et al., 2002)*.

3.1.1 Realistic Phantoms

At one extreme, anthropomorphic phantoms were used for development near the start to be sure that real patient anatomy was foundational. A Kyoto Kagaku LUNGMAN™ was used for respiratory work: the liver plug removed, and an in-house version of the Washington University 4D Phantom *(Malinowski et al., 2007)* was used to move custom tumor objects inside the lung cavity with mediastinum inserted. A Kyoto Kagaku Pelvis was custom-modified by the vendor to insert a water tank enabling a fake prostate to move inside. Both of these phantoms are pictured in Figure 4 below.

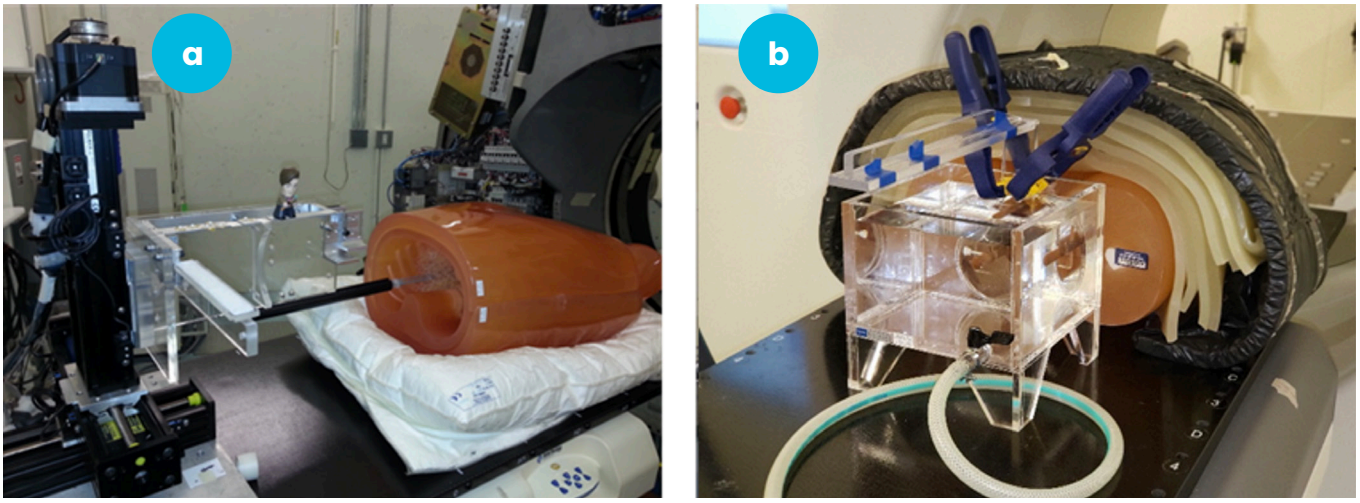

Figure 4: *Images of Kytoto Kagaku phantoms in set-ups used for testing. (a) is the LUNGMAN set-up for respiratory mode studies, and (b) is the prostate Pelvis in process of experimental setup with many layers of Superflab® for non-respiratory studies.*

These phantoms provided very realistic images and CT numbers for the tracking (*Rodríguez Pérez et al., 2018*). We attempted to make it work for a full range of clinically relevant shapes and sizes as follows:

1. **Fat Thickness / Patient Overall Size:** 95% have under 16 cm of fat (*Fryar et al., 2018*), so we made Synchrony work for at least 200 mm of fat with Superflab® in the experiments (see Figure 4).
2. **Hip:** The radiological hip thickness variation experienced by an axial treatment beam, assuming 50% cortical bone, is about 7.5 g/cm^2 to 12.5 g/cm^2. The variation was determined by assuming a proportionality to the femoral axis length variation, for which a range was provided. In effect, it was assumed that all dimensions in the hip would scale similarly from small to large in natural adult human variation.
3. **Rib Thickness:** average thickness of rib cortical bone is 6 mm with outliers less then 15 mm thick (*Yoganandan & Pintar, 1998*).
4. **Lung Tumor Size (and Composition):** 5 mm – 50 mm diameter of equivalent sphere is the range we looked at. The idea is that 5 mm is the smallest one would treat with Synchrony and larger than 50 mm is usually going up against the 20 Gy limit to the lung (Peterson et al., 2017, Allibhai et al., 2013). For tracking behavior, however, we discovered that the inhomogeneity, especially in the edges: the way the gradient of density changes near the edges was the most important part to fiducial free detection.
5. **Lung Tumor Density:** 0 HU – 100 HU was considered. It is observed that tumor density can change during treatment, often dropping (Suryanto et al., 2005, Wen et al., 2017). The algorithm fortunately is rather insensitive to overall tumor density.
6. **Alternative Fiducial or Fiducial Free Objects:** There is an interest in using natural calcifications and other agents like Lipoidol for tracking. Accuray is looking into such possibilities.

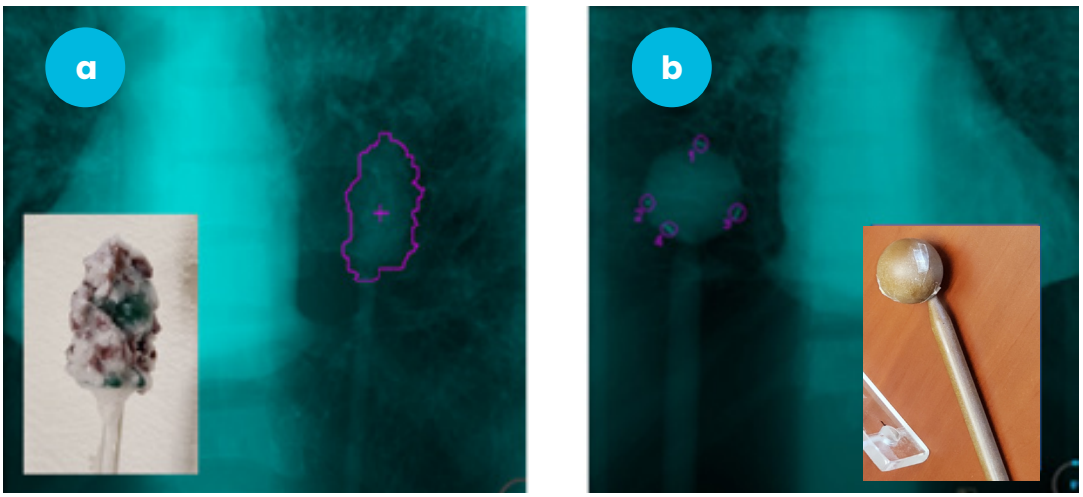

Figure 5: *Example radiographs in LUNGMAN with custom tumors: a, custom tumor made from solid water, wax and acrylic, without fiducials; b, custom solid water sphere tumor with attached gold fiducials. Inserts are photograph of the same objects in the radiograph.*

3.1.2 Phantoms for Testing

The bulk of the formal testing including dosimetry was accomplished with the ScandiDos® HexaMotion/Phantom+® system. However, we customized the Phantom+ by milling a precise hole in one acrylic quarter to accommodate a CyberKnife® Ball Cube®. We fabricated some custom ball cubes with various tumor sizes and densities and a cube of lung-equivalent material for respiratory treatments without fiducials. The span of these variations is described above.

Additionally, we fabricated a set of fake ribs made with 6 mm thickness of 100% cortical bone material for use in the assessments.

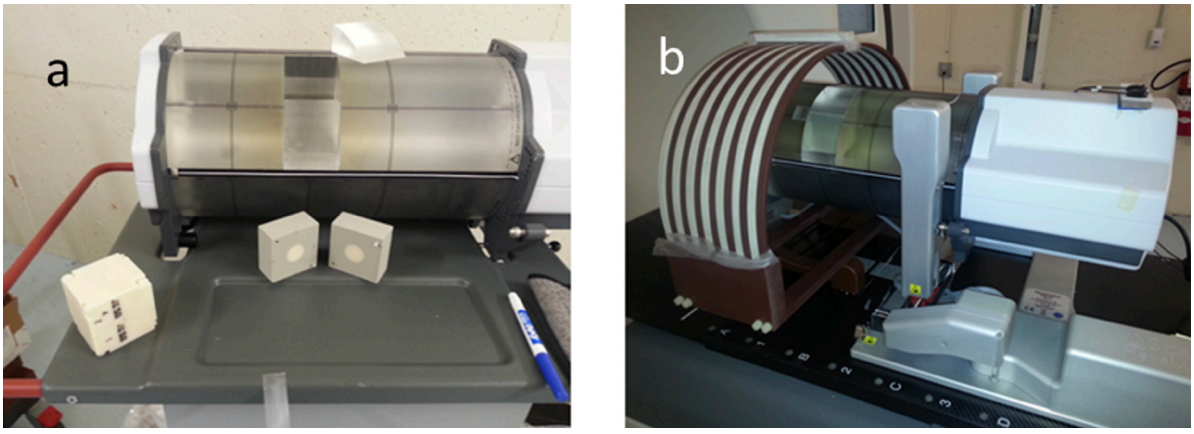

Figure 6: *Our modified ScandiDos Phantom+® with a modified quarter (a), note the custom lung cube with lung equivalent material and tumor material (75 HU, 25 mm) and also a CyberKnife Ball Cube on the left. (b) The Phantom+ is on the HexaMotion with a fake rib hoop (6 mm cortical bone alternating with solid water. The hoop structure supports many layers of SuperFlab.*

The setup shown in Figure 6 was used for testing. The kV imaging diode response can be subtracted out to check the match to the planned dose. Recently, this type of setup was used with Synchrony to pioneer patient QA procedures (Ferris et al., 2020).

3.1.3 Efficient QA Phantoms

The CIRS Dynamic Platform® (1D motion platform) with a standard Cheese Phantom and special sticks and plugs is used for acceptance testing and frequent QA. It is significantly cheaper than the system used for formal testing, and it does allow for motion axially and longitudinally with a simple shift in angle on the couch. One can use motions that stress the system and would allow for a worst case error, or one can use measured patient motions. A film with ion chamber can be used for absolute dose measurement. For tracking assessment only, one can use cross-correlation analysis on motion waveforms that are unique at all times (such as shown in Figure 7d). Then the tracking fidelity can be attained with RMS error from the lag of a cross-correlation between the input phantom instruction and the position vector the system calculates. Typically, with motions and plan as shown in Figure 7, deviations from specified performance will be noticeable on the films by the eye.

The suggested PTV shape is a ring, the same shape as described in the first IMRT paper (Brahme et al., 1982). It is sensitive to deviations in delivery fidelity because highly weighted beamlets to carve out the central avoidance also must pass through the PTV at every angle the same way. It is very sensitive to misalignments after it is optimized.

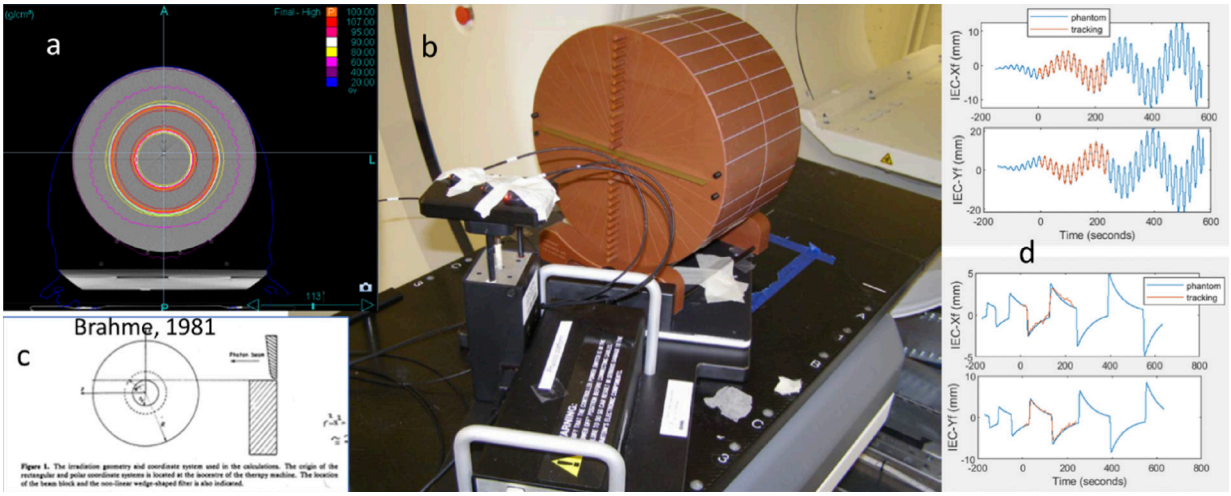

Figure 7: *The QA setup used during ATP to verify the system. (a) A sensitive plan: full concavity, equal from every direction. (c) The first IMRT paper used same shape. Note that high weighted beamlets shoot through the PTV at every angle to carve out the center with unifom dose in PTV. The optimizer works hard to match the beams, and motion throws it all off easily. The phantom is angled at 30 degrees to require MLC shifts and jaw shifts for the motion (b). The non-respiratory are composed of jumps and drifts mimicking a range of prostate-like motion. The motion for respiratory modes are like drifting oscillations.*

3.2 Formal Synchrony® End-to-End Testing

Over 30 types of end-to-end system tests ("physics testing") focusing on tracking and dosimetric performance were performed as part of the formal assessment of Synchrony performance. A few example summaries of test results are provided here. Physics testing varied conditions of the target size (a few cm to 8 cm), location (on-axis to > 20 cm off-axis), doses (2 Gy to 7 Gy), all CT orientations, and planning parameters like pitch, modulation factor, snapshot angles, etc. Tumor and prostate motions were also varied and included both challenging big steps and drifts as well as realistic cases from actual patients. For realistic cases, motions were compared to large and average real patient motions (*Huang et al., 2015*).

3.2.1 Physics Tests Results Summary

On average, over the tests, RMS tracking error values were <1 mm and well-under the design requirement of 1.5 mm: for tracking. For synchronization dose targeting and dosimetry, we used film and the Phantom+ diode arrays. The gamma metric *(Low et al., 1998)* and dose differences were the quantities used to evaluate the ability of the beam steering to provide the calculated dose.

Errors in the non-respiratory mode are mostly Gaussian with a width the size of the planning CT resolution and centered about the planned position if well-commissioned, but also with a small tail of larger errors for a short time. These tail errors are mostly related to the limitation of monoscopic view for the snapshot imaging.

Errors in respiratory modes tend to be dominated by uncertainties in the correlation model. Over many breathing cycles though, the errors tend also to a Gaussian shape but with widths that can be larger than a voxel size; often the minor radius of a hysteresis curve of the correlation model has most of the errors, especially if the major axis is more aligned with IEC-Y.

The radiograph diode response was subtracted from total diode response that has both MV and kV responses in order to get just the MV response to compare with the plan. The subtracted response does not exactly correspond to the kV dose because the diode array overresponds at lower energies.

3.2.1.1 Core Dosimetric Tests

There are four core dosimetric tests for each modality. They all use cylinders of various sizes, length, and positions. Tumor motion and other quantities are varied as mentioned above. See Table 1 for a summary of the cases and the results.

Dose Test	Plan Type	Dose/Fx (Gy)	Motion	RMS error (mm) (a)	Aver. gamma | Max gamma | % points passing (b)	Median % dose difference from plan in PTV
fid1	Patient, central	2	Drifts	0.23	0.16 | 0.74 | 100	-0.4
fid2	Patient, 5 cm off-axis	4	Jumps & Drifts	1.47	0.25 | 0.59 | 100	-1.1
fid3	Patient, 10 cm off-axis	6	Realistic	0.83	0.15 | 0.53 | 100	0.3
fid4	Patient_QA, central	7	Realistic	0.66	0.17 | 0.64 | 100	-1.6
fidRes1	Patient, 10 cm off-axis	2	+/- 7 mm cos6	0.17	0.25 | 0.71 | 100	0.8
fidRes2	Patient, 5 cm off-axis	4	5D realistic	0.46	0.16 | 0.51 | 100	0.9
fidRes3	Patient, 1 cm central	6	+/- 7 mm cos6	0.37	0.18 | 0.56 | 100	0.0
fidRes4	Patient_QA, >10 cm off -axis	6.4	5D realistic	0.58	0.30 | 0.93 | 100	0.8
lungRes1	Patient, 10 cm off-axis	2	+/- 7 mm cos6	0.29	0.35 | 1.04 | 99.1	-1.9
lungRes2	Patient, 5 cm off-axis	4	5D realistic	0.39	0.24 | 0.56 | 100	-1.3
lungRes 3	Patient, 1 cm central	6	+/- 7 mm cos6	0.25	0.29 | 0.78 | 100	0.3
lungRes4	Patient_QA, >10 cm off -axis	6.4	5D realistic	0.38	0.27 | 0.91 | 100	0.1

Table 1: *Dosimetric Test Results. Note: (a) Must stay < 1.5 mm; (b) Gamma test criteria for non respiratory modes: >95% of the diode measurements within the 50% isodose line agree with the plan using a gamma criterion of 5%/4 mm. Gamma test criteria for respiratory modes: We need >95% of the diode measurements within the 50% isodose line agree with the plan using a gamma criterion of 3%/3 mm. Definitions: fid = Fiducial Tracking™; fidRes = Fiducial Tracking™ with Respiratory Modeling™; lungRes = Lung Tracking™ with Respiratory Modeling™.*

3.2.1.2 Core Targeting and Tracking Tests

Each flavor of Synchrony® had its own tracking and targeting test. Even though tracking analysis was performed on every test, this test tied it to targeting the beam – a test of the beam steering described earlier. The tracking target and the dose target are the same in this test, both of which are in the Ball Cube. The plan had tuning structures to tighten the dose gradient as much as possible. See Table 2.

Targeting and Tracking Test for	Plan Type	Dose/Fx (Gy)	Motion	RMS error (mm) (a)	3D offset (mm) (b)
fid	Patient, central	4.2	Realistic	0.37	0.50
fidRes	Patient, central	4.2	+/-7 mm cos^6	0.37	1.1
lungRes	Patient, central	4.2	+/-7 mm cos^6	0.45	1.5

Table 2: *Tracking & Targeting Test Results. Note: (a) Must stay < 1.5 mm; (b) Centroid shift of the 70% isodose line must stay < 3.0 mm for respiratory and < 2 mm for non-respiratory; Definitions: fid = Fiducial Tracking™; fidRes = Fiducial Tracking™ with Respiratory Modeling™; lungRes = Lung Tracking™ with Respiratory Modeling™*

3.2.1.3 Pause-Resume & Interruption-Completion Tests

These tests involved plans that were sensitive to a mis-junction and are intended to confirm that the dose is delivered properly in cases where the treatment fraction has been interrupted in some manner. There are two cases: 1) "pause-resume" in which the treatment stops but the system remains in full operation and can be resumed by the user. Such pauses can be initiated by the user or by the system itself when Synchrony modeling parameters exceed the set range for values. 2) "interruption" in which the system stops completely and can only be resumed by reloading the patient or restarting the system. Such interruptions can be initiated by the user (by pressing the "stop" button on the status console) or by the system if some internal system parameter falls out of tolerance. With both the softer pause-resume and with the harder interruption, the delivery was able to recover as if the pause or interruption never happened. See Table 3 for some results.

Test	Plan Type	Motion	Aver. gamma | Max gamma | % points passing (a)	Median % dose difference from plan in PTV
Fid – Pause-resume	Patient, central, 2.5 Gy/Fx	Drift	0.26 | 1.13 | 99.7	1.2
fid – Interrupt-complete	Patient, central, 2.5 Gy/Fx	Drift	0.30 | 0.97 | 100	1.5
fidRes – Pause-resume	Patient, central, 2.5 Gy/Fx	+/-7 mm cos^6	0.30 | 0.95 | 100	1.5
fidRes – Interrupt-complete	Patient, central, 2.5 Gy/Fx	+/-7 mm cos^6	0.30 | 0.97 | 100	1.5
lungRes – Pause-resume	Patient, central, 2.5 Gy/Fx	+/-7 mm cos^6	0.30 | 0.95 | 100	1.5
lungRes – Interrupt-complete	Patient, central, 2.5 Gy/Fx	+/-7 mm cos^6	0.30 | 0.97 | 100	1.5

Table 3: *Most Recent Pause-Resume and Interruption-Completion Test Results. Note: (a) for pause-resume / Interruption-completrion, we need no visual evidence of a misjunction, and the following: non-respiratory: >95% of the diode measurements within the 50% isodose line agree with the plan using a gamma criterion of 5%/4 mm; no visual evidence of a misjunction; respiratory: >95% of the diode measurements within the 50% isodose line agree with the plan using a gamma criterion of 3%/3 mm; and again. Definitions: fid = Fiducial Tracking™; fidRes = Fiducial Tracking™ with Respiratory Modeling™; lungRes = Lung Tracking™ with Respiratory Modeling™.*

3.2.2 Fiducial Tracking Test Result Example

This fiducial tracking test is of note for having a particularly challenging prostate-like motion. The tracking RMS error will of course be sensitive to the number and size of jumps. In this test, there are some big successive jumps combined with orthogonal drifting. The magnitude and intensity of the motion is certainly larger than most real prostate motions. The system stays within 1.5 mm (1.47 mm is the RMS tracking error), and it passes the gamma tests for dose. The structure is a small cylinder 5 cm off-axis getting 4 Gy/Fx. The results are shown in collage in Figure 9 below.

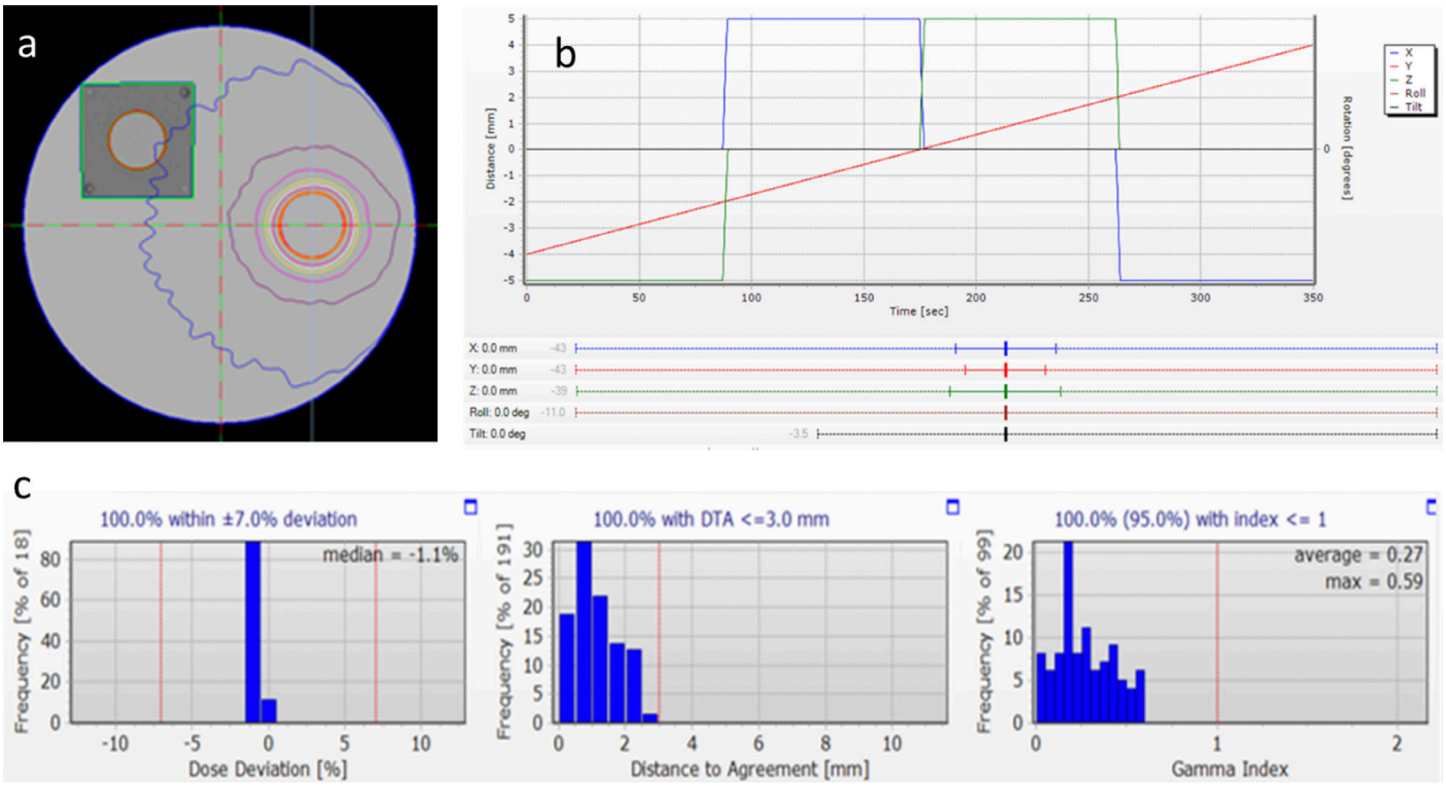

Figure 8: *Example Fiducial Tracking™ test result collage. (a) shows the dose plan – one can see the tracking structure is separate (the Ball Cube). The programmed motion from the ScandiDos HexaMotion software. Finally, the dose results from the Scandidos Phantom+ software: 100% of the points the diode measurements were within the 50% isodose line agree with the plan using a gamma criterion of 5%/4 mm; 100% of the diode measurements within the 100% isodose line agree with the plan to within 7%.*

3.2.3 Fiducial Tracking with Respiratory Modeling Test Result Example

This example is very close to what a Patient_QA procedure would be for many clinics. It is a lung case far off-axis (>10 cm). The dose is 6.4 Gy/Fx. It passed the dose tests and the tracking RMS error was 0.58 mm for the whole treatment. The motion used is worth noting. It is a mock trace generated to match a realistic hysteresis (Seppenwoolde et al., 2002) and so needs the 5D model. See Figure 9 below for a visual description of the motion. This might be similar to a patient coughing, but as long as the internal motion stays correlated with the LED markers on the surface, the system will not interrupt. One can see that the jaw movements are well-tuned.; the dose, even way off-axis, matches the plan well.

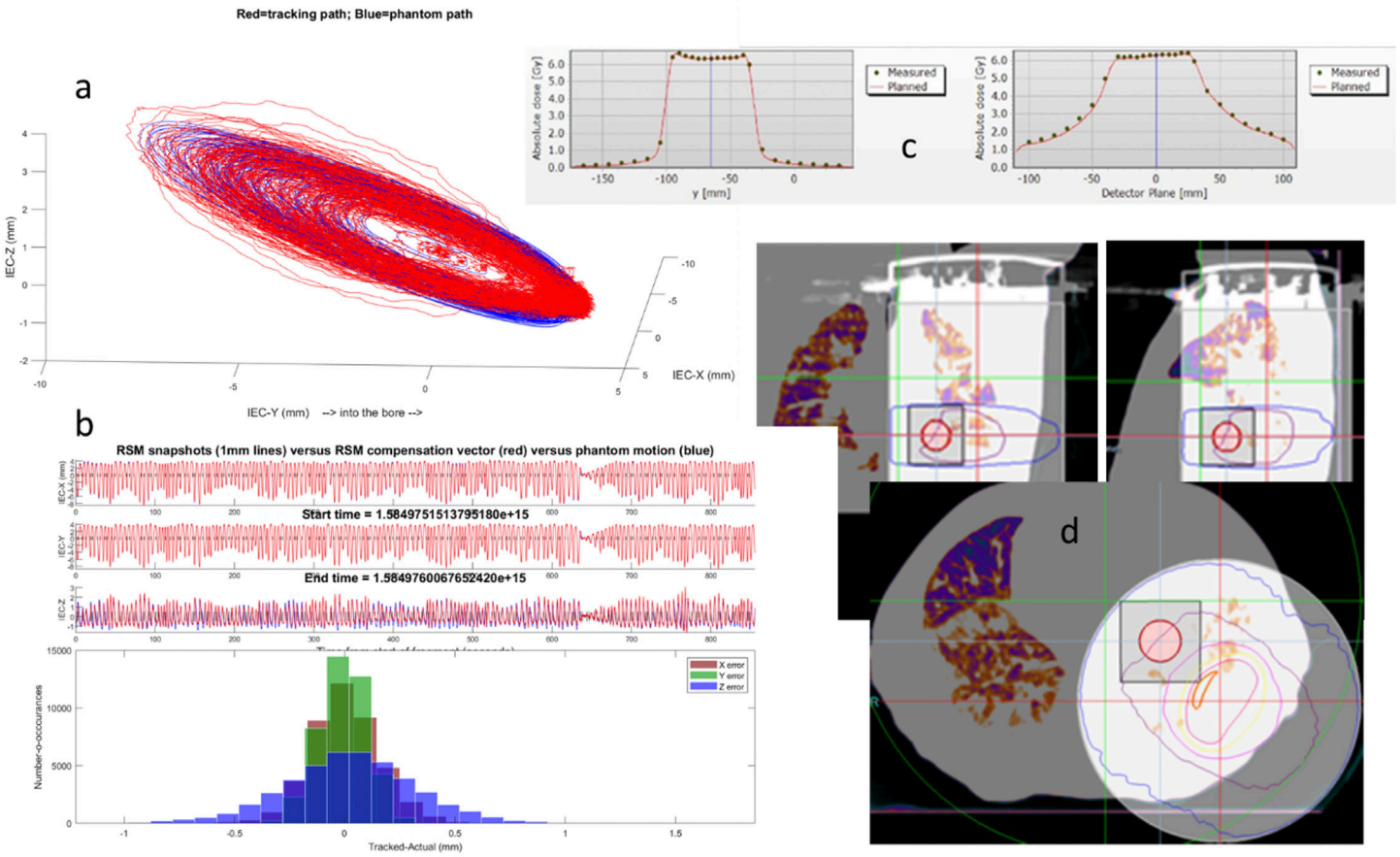

Figure 9: *Example Fiducial Tracking with Respiratory Modeling™ test result. (a) the 3D movement of the phantom (blue) and the tracking result (red). (b) The time behavior of this trace in each direction: IEC-X, IEC-Y, and IEC-Z. Same color scheme but note that the overlay is so good it is hard to tell which is which in the X and Y overlays. Most errors were in the minor axis, Z. in (c), notice the measured points versus the red line of the plan. The plan itself (d) is shown in all three planes. Notice the green laser lines indicate isocenter at their intersection. Gamma test passes with 100% of the diode measurements within the 50% isodose line agree with the plan using a gamma criterion of 3%/3 mm.*

3.2.4 Lung Tracking with Respiratory Modeling Test Result Example

A final example shows how one can use the CyberKnife® Ball Cube with film. This time the tracking target is the dose target as would typically be the case in a patient treatment. (Note that in the previous examples, the tracking and dose target were separated by design to allow for the diode array not to interfere with the tracking object). The dose here was 4.2 Gy/Fx, and the motion was a +/-7 mm $\cos^6$ (centered on the mean). The RMS tracking error for this case was 0.45 mm. It passed the targeting test as well, the centroid of the 70% isodose line was within 3 mm of the static case registered at the time-averaged position of the motion. See Figure 10.

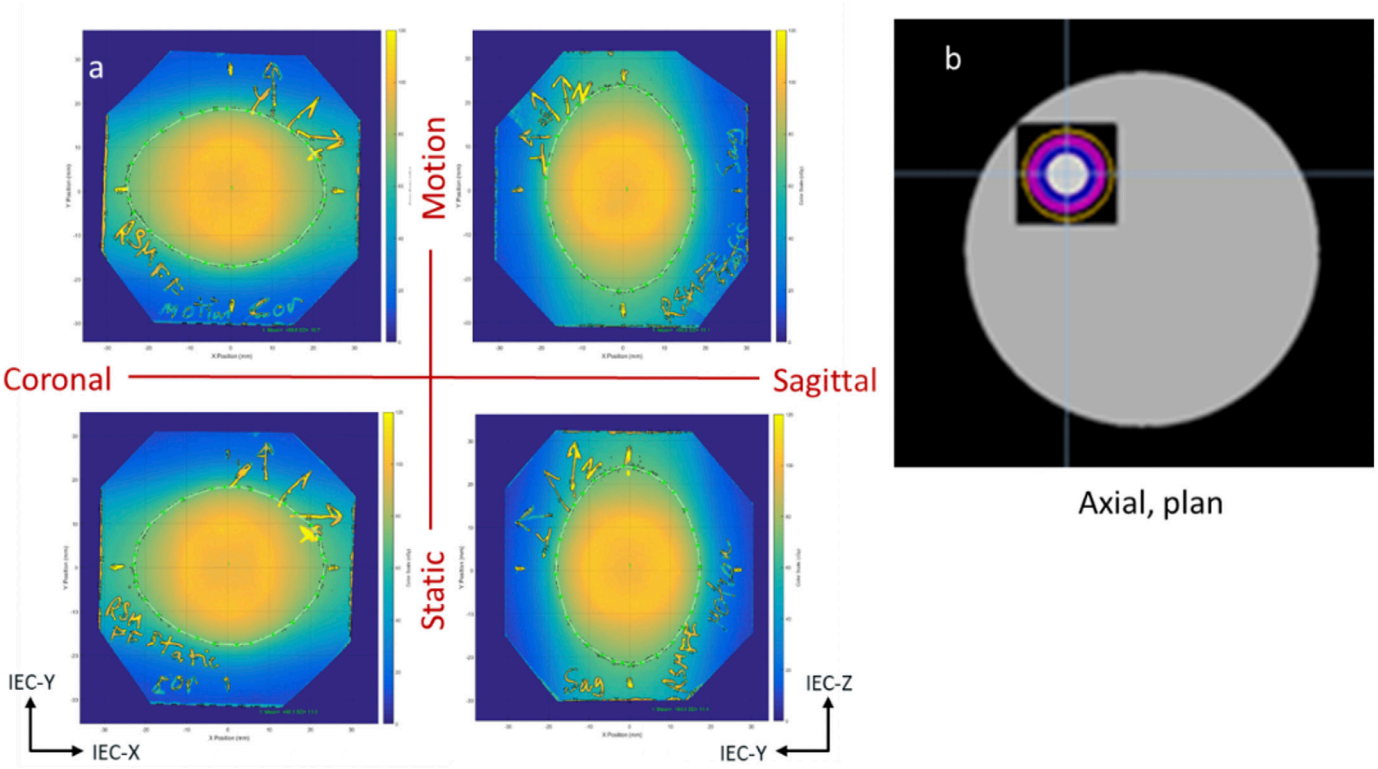

Figure 10: *Example Lung Tracking with Respiratory Modeling™ test result: Targeting, looks at the position of the beam itself. (a) 4 panel shows example scanned films that had been inserted into the CyberKnife Ball Cube, then inserted into the modified custom quarter of the phantom+. The plan's axial slice with isodose lines shown in (b).*

4. HUMAN TREATMENT EXAMPLES

These two examples and other results are published from the team at the Froedtert Hospital & The Medical College of Wisconsin (Chen et al., 2020). The first is a hypofractionated Stereotactic Body RadioTherapy (SBRT) lung metastatis case without the use of any fiducials – just that patient's particular lung anatomy with its tumor. The other case shows a prostate treatment using the non-respiratory Fiducial Tracking mode. In both cases, a significant margin reduction leads to PTVs that are reduced by about a third, often allowing for a boosted dose.

4.1 Fiducial Free Lung SBRT

The dose was 50 Gy in 5 fractions delivered to this lung metastisis. The PTV was 29.5cc using only a 5mm isotropic margin, which was a 32% reduction in PTV volume compared to a delivery without motion synchronization due to this smaller margin. See Figure 11 below for images of the plan and the kV snapshots that the Radixact® System acquires with one of them including a delineation of the target. The tracking system had no trouble finding this tumor. The beam-on time was 9 minutes and 54 seconds. The complete time that the patient was in the room was 20 minutes. During the treatment, the patient had no restraints and breathed normally. Nothing was implanted. Note that a gating treatment would typically be three times longer.

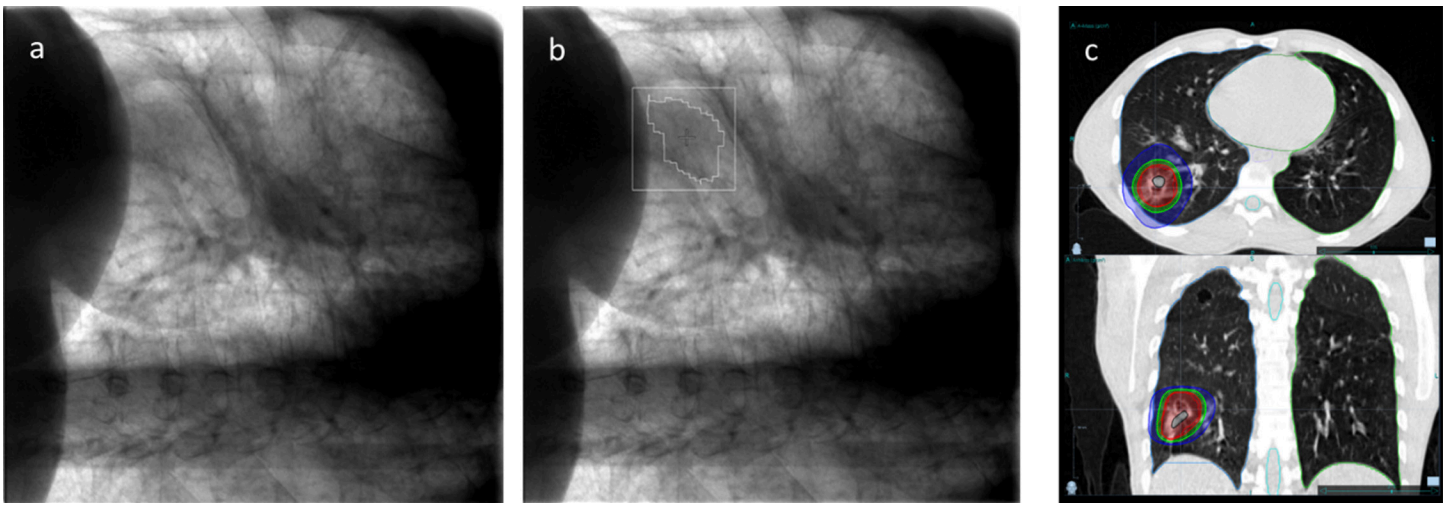

Figure 11: *Images from the Lung Tracking with Respiratory Modeling clinical case example. Images (a) and (b) are the same except that (b) renders the object deliation from planning overlaid on the latest kV snapshot – the algorithm finds this object easily. Images (c) are from the planning station showing dose calculation overlaid with the planning CT scan.*

4.2 Prostate

The dose was 70 Gy in 28 fractions delivered to the prostate. The PTV was 80.1cc with margins varying from 3 to 5 mm. If not using Synchrony, this clinic would typically use 5-8 mm sized margins ending up with a 130cc sized PTV instead of the much smaller one used here. In this case, the beam on time was 5.5 minutes, and the total time in the room was 15 minutes. The kV snapshots from each angle are shown in Figure 12.

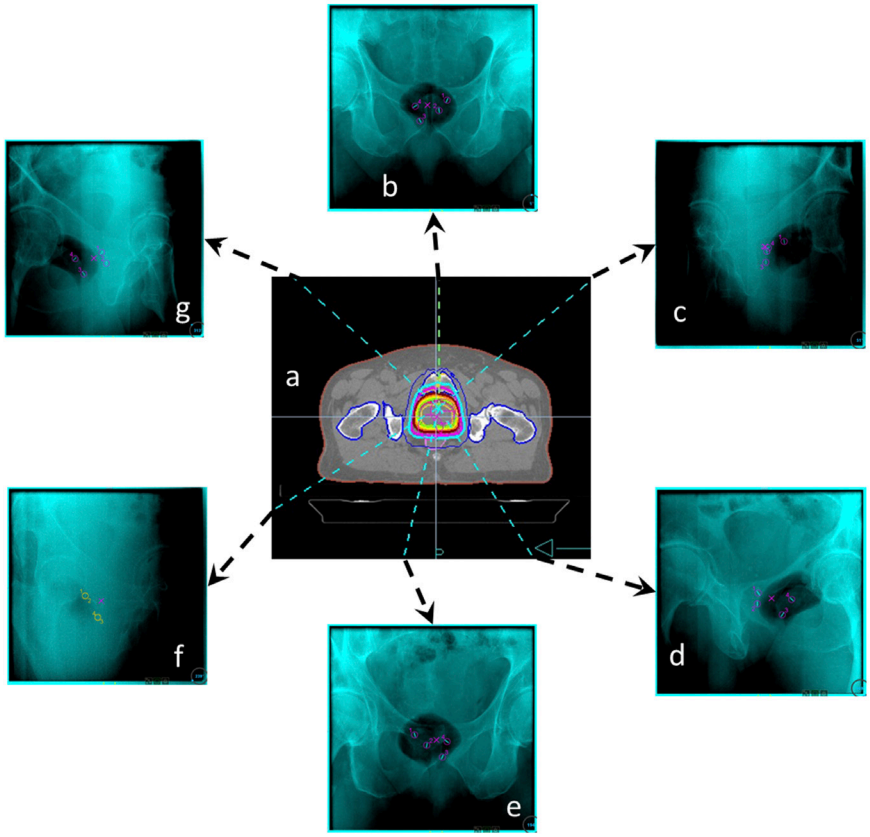

Figure 11: *The central image (a) is from planning, and the surrounding images (b)-(g) are from the TDC showing kV snapshots for each angle. The fiducials circled in magenta are found, but in one image, (f), they are not. In (f), the yellow circles about each fiducial show that the system is not confident that it found them.*

5. CONCLUSION

Synchrony® on Radixact® is a fully automated dynamic system in which the planned delivery of radiation for the given treatment fraction is adapted in real-time to the observed motion of the tumor inside the patient. The user drives this dynamic system and remains in control with live updating quantities that indicate 2D tracking fidelity, 3D overall model uncertainty, model age, and other parameters to assess tracking and modeling fidelity. The system automatically and actively tracks the object, steers the beam, and adjusts its width and strength to a self-adapting live modeled position that remains synchronized with the tumor motion through a correlation to a high time resolution signal. For respiratory motion, LED markers and a camera provide high time resolution patient surface measurements. A sophisticated model then correlates these surface movements to the tumor or fiducial motion inside the patient with periodic low dose kV x-ray snapshots. The result is an algorithm that maintains planned dose to the tumor even when the tumor is moving and the dose rate itself is modulated. By contrast, gating does not modify the beam at all, but only turns it off and on to select time ranges that accept a tolerated level of blur. Synchrony takes blur to a minimum by following even small motions in real time through respiratory modeling while remaining unencumbered by system latency.

The system testing leveraged a wide range of phantom environments and objects to track to assess the overall system performance. Care was taken to accommodate realistic clinical radiological thickness and other size and composition ranges as well as classic QA phantom idealized shapes and materials. Throughout this process, QA procedures were developed. With phantom testing, 100% of our dosimetric tests passed, and the average RMS tracking error was less than 0.5 mm. Clinically, one can expect to stay on the order of the planning CT resolution for averaged tracking errors. The RMS error here would represent the blurring size and it is now very small. The residual blurring is now more related to resolution than it is to the particular motion.

As a result, one should consider that motion is no longer the major factor for margin size in lung cases. Initial clinical sites are finding this to be true. Because of margin reduction, the PTV volume is commonly reduced by about a third. The field is indeed at a tipping point (Keall et al., 2018), and Synchrony® is already here now.

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