ACCURAY

Hypofractionation In the Age of Value-based Care

Today, Tomorrow and the Future
Are You Ready?

Executive Summary

As healthcare systems around the world increasingly adopt the value-based care approach, the field of oncology – facing the burden of increasing cancer rates and high cost of care – has emerged as a prime target for uncovering new efficiencies in care and cost. As one of the most cost-effective cancer treatment modalities, radiation therapy is now a central element of value-based cancer care. In particular, hypofractionated and ultra-hypofractionated radiation therapy – increasing dose per fraction to enable significantly fewer overall treatments – holds great promise in the age of value-based care.

Realizing this potential on a wide scale requires a new standard of functionality in treatment delivery systems and their accompanying software. To confidently increase dose per fraction, clinicians need the ability to maintain sub-millimeter accuracy and precision throughout treatment delivery at every step: from identifying the target location in the body, to automatically detecting and reacting to target motion, to accurately re-pointing the beam in real time to minimize margins. Between treatment fractions, clinicians must have the tools to efficiently make the appropriate plan adjustments to account for anatomical changes. But to manage increasing demand and growing economic pressures, this increased precision cannot come at the expense of system versatility or delivery efficiency. The new standard in radiation therapy will be a system that can deliver the highest level of accuracy and precision to both stationary and moving targets – with the workhorse versatility to treat the full range of clinical indications efficiently.

The Growing Cancer Burden Challenges Healthcare Systems Worldwide

The shift to value-based reimbursement is complicated by the convergence of an increase in demand – led by aging Baby Boomers – and an urgent need to control rising healthcare costs.

The global cancer incidence is predicted to rise from 14 million today to 25 million by 2030.[1]

The worldwide economic impact of cancer – estimated at $1.6 trillion in 2010 – will see a corresponding and concerning rise.[2]

[1] *Atun et al. Expanding global access to radiotherapy. Lancet Oncol 2015; 16:1153-86.*
[2] *Stewart BW, Wild CP, editors. World cancer report 2014*

Radiation Oncology Takes the Spotlight

Though radiation therapy (RT) has been widely used in cancer care for decades, this highly cost-effective treatment modality is rapidly becoming a focus of value-based cancer care. Estimates suggest that 50 to 60 percent of diagnosed cancer patients will require some form of radiotherapy. In short, this means that a significant portion of the growing global cancer burden falls on the shoulders of the world's radiation oncologists, radiation therapists, and medical physicists.

The challenge now is to identify new treatment tools and protocols that deliver optimal patient outcomes – both objectively (e.g., long-term cancer control) and subjectively (e.g., patient comfort and convenience) – while maximizing treatment efficiency, allowing radiation oncology teams to provide high quality treatments to more patients, in less time, at a lower cost.

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1 Atun et al. Expanding global access to radiotherapy. Lancet Oncol 2015; 16:1153-86.

Hypofractionation Offers Promising Value-based Care Protocols

A growing body of clinical evidence supports hypofractionated RT – delivering a higher dose per fraction across fewer total fractions. Hypofractionated RT has been proven to deliver clinical outcomes as good as conventional fractionation, while dramatically reducing both the number of treatments and the total cost of care. New treatments range from small increases in dose above 2 Gy per fraction all the way to ultra-hypofractionated (AKA, extreme hypofractionated or hyperfractionated) delivery up to and including stereotactic radiosurgery (SRS), stereotactic radiation therapy (SRT), stereotactic body radiotherapy (SBRT), and stereotactic ablative radiotherapy (SABR). New guidelines, protocols and standards continue to emerge, each further increasing dose per fraction with fewer fractions for a given indication.

Healthcare payers, seeing the clinical efficacy of increasingly hypofractionated treatments, recognize the potential cost savings and increasingly reward institutions practicing hypofractionated treatment. In existing value-based care markets, fewer treatments and a lower cost of care lead to higher gross margins per patient and greater profitability for both payers and providers.

Patients, too, benefit from the efficiency of hypofractionated RT. Fewer treatments means fewer clinical visits and a faster return to family, friends and other aspects of life.

Between the global shift to value-based care and the growing cancer burden worldwide, hypofractionated RT gives payers and radiation oncologists a powerful tool for treating significantly more patients at a significantly lower cost, protecting margins for the practice.

1 Buyyounouski, M. K., Balter, P., Lewis, B., D'Ambrosio, D. J., Dilling, T. J., Miller, R. C., ... & Konski, A. A. (2010). Stereotactic body radiotherapy for early-stage non-small-cell lung cancer: report of the ASTRO Emerging Technology Committee. International Journal of Radiation Oncology• Biology• Physics, 78(1), 3-10.

2 Freedman, G. M., Anderson, P. R., Goldstein, L. J., Ma, C. M., Li, J., Swaby, R. F., ... & Morrow, M. (2007). Four-week course of radiation for breast cancer using hypofractionated intensity modulated radiation therapy with an incorporated boost. International Journal of Radiation Oncology* Biology* Physics, 68(2), 347-353.

2 Freedman, G. M., Anderson, P. R., Bleicher, R. J., Litwin, S., Li, T., Swaby, R. F., ... & Morrow, M. (2012). Five-year local control in a phase II study of hypofractionated intensity modulated radiation therapy with an incorporated boost for early stage breast cancer. International Journal of Radiation Oncology* Biology* Physics, 84(4), 888-893.

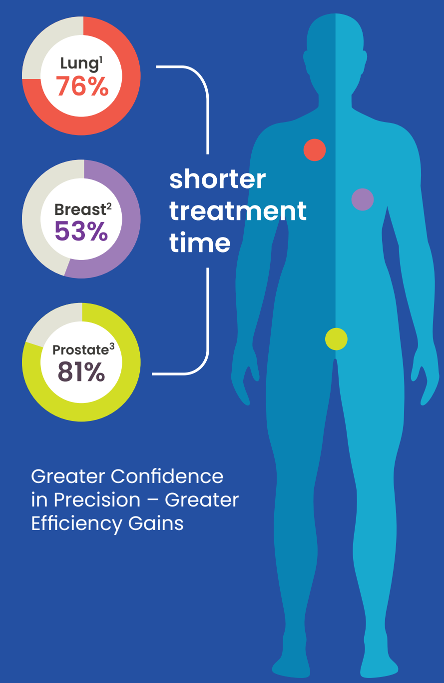
2 Jagsi, R., Griffith, K. A., Boike, T. P., Walker, E., Nurushev, T., Grills, I. S., ... & Pierce, L. J. (2015). Differences in the acute toxic effects of breast radiotherapy by fractionation schedule: comparative analysis of physician-assessed and patient-reported outcomes in a large multicenter cohort. JAMA oncology, 1(7), 918-930.

3 Shaikh, T., Li, T., Handorf, E. A., Johnson, M. E., Wang, L. S., Hallman, M. A., ... & Chen, D. (2017). Long-term patient-reported outcomes from a phase 3 randomized prospective trial of conventional versus hypofractionated radiation therapy for localized prostate cancer. International Journal of Radiation Oncology* Biology* Physics, 97(4), 722-731.

3 Meier, R. M., Bloch, D. A., Cotrutz, C., Beckman, A. C., Henning, G. T., Woodhouse, S. A., . . . Kaplan, I. D. (2018). Multicenter Trial of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer: Survival and Toxicity Endpoints. International Journal of Radiation Oncology*Biology*Physics,102(2), 296-303. doi:10.1016/j.ijrobp.2018.05.040

A Dramatic Reduction In Cancer Treatment Times

Hypofractionation typically reduces treatment times dramatically for a number of different indications:



Greater Confidence in Precision – Greater Efficiency Gains

RADIOTHERAPY TREATMENT OF PROSTATE CANCER

Ultra-Hypofractionation
≤5 FRACTIONS

Conventional Fractionation
29–39 FRACTIONS

Barriers to Success in Hypofractionated RT

Considering the growing body of clinical evidence supporting its efficacy and efficiency, adoption of hypofractionated RT remains relatively low. A growing number of radiation oncologists recognize hypofractionation as the future of the field, yet find themselves facing two challenges:

Confidence In Precision

Existing treatment delivery platforms typically fail to give the confidence necessary to deliver significantly higher dosage per fraction. In particular, the lack of true real-time motion tracking and correction means clinicians cannot be fully confident in the precision and accuracy of high-dose delivery for the many indications where the target moves during the delivery of a fraction.

Lacking fully integrated, automated, adaptive RT capabilities to account and correct for translational shifts, rotations and anatomic changes such as tumor shrinkage, organ deformation, and weight loss, clinicians don't have the tools to efficiently make the required plan adjustments between treatment fractions to deliver high radiation doses.

Treatment Versatility & Efficiency

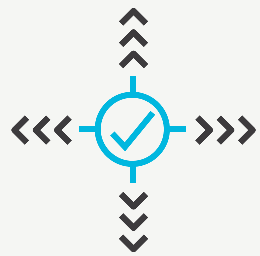
Those few existing technologies that do offer motion compensation capabilities fail to deliver sufficient treatment versatility with the required delivery efficiency. In the few instances where inter-fraction plan adaptation is possible, it is time-consuming and cumbersome. At a time when operational efficiency and economic outcomes are paramount, radiation oncology practices of all sizes struggle to justify the investment in inefficient technologies.

Realizing The Full Potential Of Hypofractionated RT

While these limitations frustrate many radiation oncologists today, technologies already exist that overcome these barriers – enabling both highly precise and efficient treatment delivery with a versatile system. However, fully realizing the potential of hypofractionated RT – and bringing these benefits to patients around the world – requires a shift in thinking around three existing paradigms:

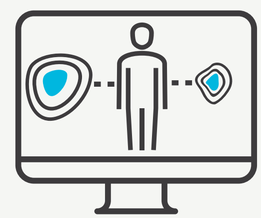
1

Motion Matters –
More Than Ever
The Need for Next
-Generation Precision



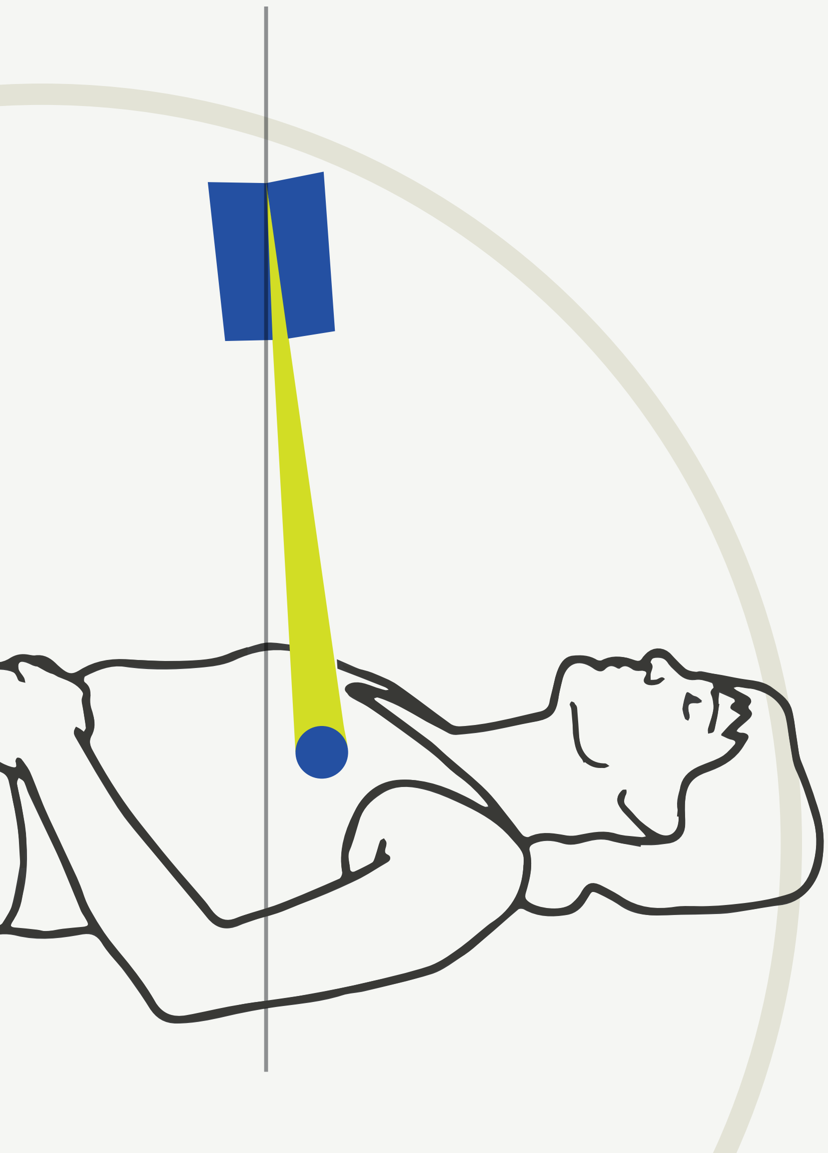
2

Motion Management
Motion Compensation vs.
Motion Synchronization



3

Adaptive Planning
Adapt the Plan to the
Patient – Not the Patient
to the Plan



1 Motion Matters

– More Than Ever

Confidently delivering the prescribed dose to the target while minimizing margins to protect healthy surrounding tissues is always the top priority in radiation oncology. However, as the dose per fraction is increased, precision and accuracy become even more critical for ensuring positive patient outcomes. Cancers where anatomical motion can cause the target to gradually drift (common for intracranial and spine targets), unpredictably shift (common for prostate and gynecological targets) or move rhythmically with respiration (common for abdominal and thoracic targets) significantly amplifies the challenge of precise hypofractionated or ultra-hypofractionated dose delivery.

Accurately tracking random target motion or anticipating cyclical target motion is only part of the equation when dealing with targets that move. How the delivery system accounts for, and reacts to, the detected motion during a treatment delivery will become the defining capability of successful hypofractionated and ultra-hypofractionated RT. Moreover, as hypofractionated RT increasingly emerges as the new standard for many clinical indication, practices, those with sophisticated motion management capabilities will likely expand their patient base and reach profitability while those without will find themselves playing catch-up.

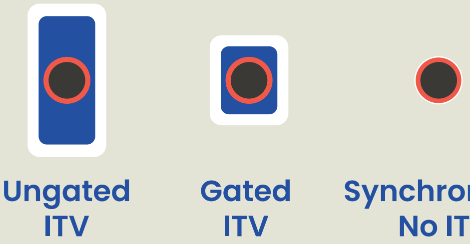
2 Motion Management

Motion Compensation

Motion management is not a new topic in radiation oncology. Yet today, most practices and systems try to compensate for motion, acting to neutralize or correct for it – as if it is a deficiency or abnormality. Others try to make up for motion by exerting an opposite force or effect – as if the motion is something unwelcome. Most commonly, an internal target volume (ITV) is used. ITVs add a margin to compensate for suspected movement, but result in healthy tissue receiving an unwanted and unneeded dose.

Further attempts to compensate for motion aim to reduce the ITV size. These techniques include attempting to immobilize the patient by employing restraints to dampen movement or keep the target in place once positioned under the treatment beam. Other techniques attempt to deliver treatment only when the target moves into the treatment beam "window." This generally involves asking the patient to hold their breath to properly position the target. Yet another technique is "gating" the treatment – attempting to turn on the radiation beam only when the target is predicted to be in the path of the beam during respiration. Still other techniques simply detect movement, stop the treatment, and require the patient to be repositioned so the new target location will be under the treatment beam.

ITVS BY APPROACH



GTV (black), CTV (red), ITV (blue), PTV (white)

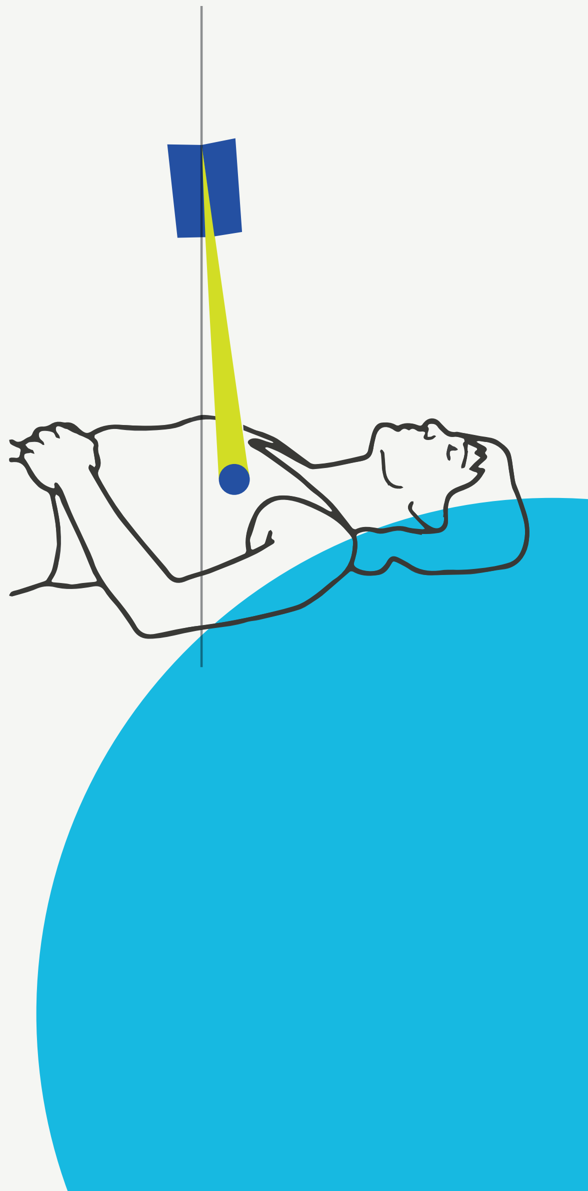
In other words, the industry-standard approach to motion management is to move the patient (and target) to the stationary beam. There are several problems with this approach: 1) healthy tissue still receives unwanted elevated dose because of target movement, 2) treatment delivery becomes inefficient, and 3) in many cases, the patient is asked to alter their normal behavior (breath-hold) making them uncomfortable and uneasy. These shortcomings make the move-the-patient-to-the-beam approach incompatible with the operational efficiency and patient satisfaction required in a value-based healthcare landscape.

To fully enable hypofractionated RT and adapt to the world of value-based care, it's time to shift the motion management paradigm. Instead of moving the target to the beam, the beam should move with the target. Rather than attempting to compensate for motion, treatment delivery should be fully synchronized with normal motion.

2 Motion Management

Motion Synchronization & Real-time Adaptation

While motion compensation attempts to stop target motion or treatment delivery during certain phases of the motion, motion synchronization allows target motion to happen naturally. Motion synchronization tracks, detects and – most importantly – takes action to synchronize and adapt the delivery beam to the target position as the target moves. Simply put, motion synchronization is real-time adaptive radiation therapy, in which the treatment delivery is adapted to measured or predicted target motion. The result is that dose can be continuously and efficiently delivered to the target while it moves – with the accuracy and precision required for hypofractionated RT with tight margins and steep dose gradients.



With motion synchronization, target tracking and detection is performed using either the patient's own anatomy or implanted fiducial markers, depending on the type of clinical case. For targets that move unpredictably, intrafraction imaging detects the motion, and the system immediately adapts, synchronizing the treatment beam to the detected target position.
For targets that cyclically move, the system predicts the target's anticipated position using sophisticated algorithms that model respiratory motion – and continuously updates the predictive model with the latest target position captured automatically by the delivery system, with no interruption to treatment delivery.

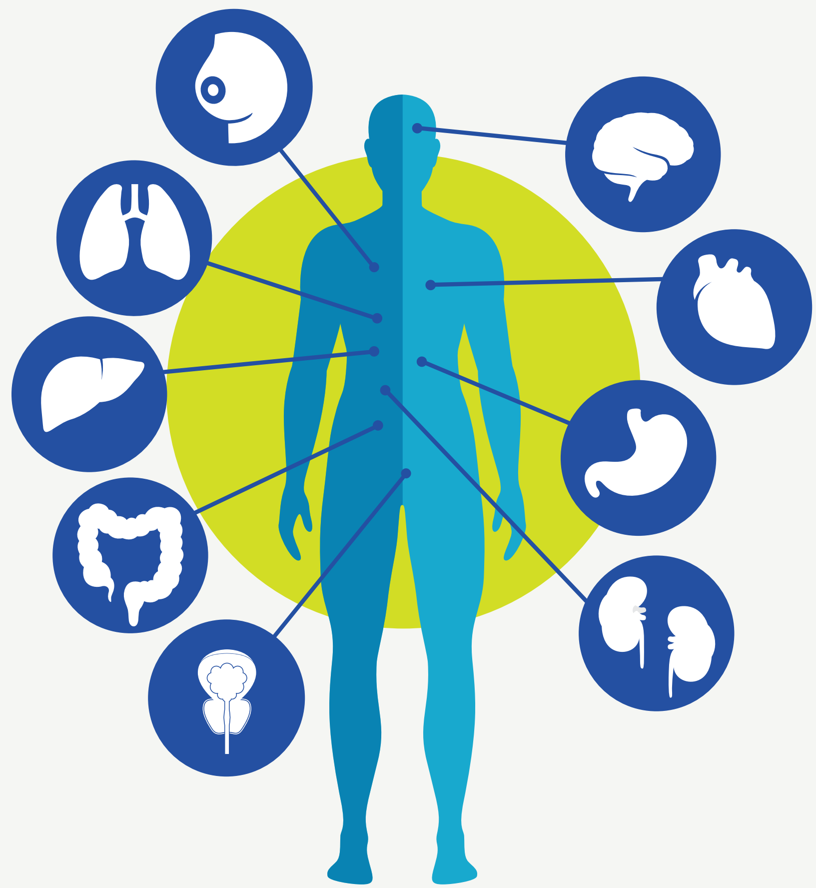
Treatment delivery adaptation and beam synchronization can occur in two ways. The linear accelerator (linac) can physically change position relative to the patient, so that it moves along with the target. This technique is employed by robotic systems where the robot precisely moves the linac head. The alternative, where it is not possible to move the entire linac, is to adjust collimation of the beam in real time, re-pointing it so that it follows the target. Ultra-fast dynamic collimation systems use high-speed multi-leaf collimators and jaws to adjust the beam and synchronize its position with the target.

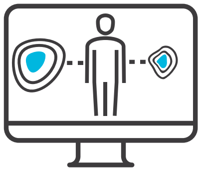
2 Motion Management

Precise, Versatile, Efficient

Conventional wisdom in the field says that these advanced motion synchronization and real-time adaptation capabilities only exist in “specialized” platforms that offer limited treatment versatility. Increasing economic pressures make practices wary of such “special” investments.

Again, it’s time to shift that paradigm. The reality is treatment delivery systems capable of motion synchronization are versatile and are able to treat any indication in the body. These machines now offer fully-featured, efficient planning and optimization systems that do not require specialized personnel to operate them. The motion synchronization and real-time adaptation capabilities of these systems are artificial intelligence (AI) driven and therefore don’t require human intervention while in operation. Most importantly, treatment delivery times associated with motion synchronization delivery systems are on par with, and in some cases faster than, conventional delivery systems on an indication by indication basis. Treatment delivery systems with motion synchronization and real-time adaptation capabilities are the only systems ready to deliver treatments that are increasingly (ultra) hypofractioned today, tomorrow, and most certainly in the future.





3 Adaptive Planning

Adapt the Plan to the Patient – Not the Patient to the Plan

Every patient is unique – and deserves highly personalized treatment. Each unique patient is also a living, breathing, often-changing individual. In fact, between treatment sessions, a patient's anatomy may change significantly. Patients gain and lose weight. Their stomach, bladder and bowel contents change. Their organs may shift, rotate or deform. Their tumor(s) may shrink, shift or rotate. Any one of these changes can have profound implications on RT treatment objectives. Yet traditional treatments rely on a single snapshot of the patient at the start of treatment, and most practices are limited in their ability to re-image patients – bound by rigid-body matching that does not account for any geometric deformations in the patient's anatomy. As a result, a plan attuned to the initial simulation can become suboptimal as the treatment progresses – rendering it unusable for hypofractionated or ultra-hypofractionated treatments.

Adaptive radiotherapy (ART) solves this deficit, using continual patient imaging to evaluate and characterize systematic and random variations – between sessions, as well as while the patient is on the table – customizing the patient's treatment plan to account for patient-specific, day to day variation in anatomy. Proven offline adaptive planning tools automatically monitor protocol-specific action levels, flagging cases for review and possible plan adaptation. Automatic recontouring accelerates the actual plan adaption, maintaining the integrity of original treatment plan objectives to ensure tumor coverage, preserve organ at risk (OAR) doses and reduce toxicity – without placing a heavy burden on clinical teams. Online ART tools present the next frontier in adaptive planning capabilities, enabling treatment teams to dynamically change the treatment plan immediately before a treatment session – while the patient is on the table. As automated algorithms continue to improve, online ART is quickly advancing toward mainstream viability, and will drive the future of hypofractionated and ultra-hypofractionated radiotherapy.

Delivering Value-based Cancer Care Demands New Technologies

As the demands facing cancer care providers evolve, the expectations placed on cancer treatment technologies also shift. Never has this been more apparent than with the global trend toward value-based care and the corresponding trend toward hypofractionated and ultra-hypofractionated RT. As they look to simultaneously maximize treatment efficacy and efficiency, RT practitioners increasingly recognize that conventional technologies simply cannot deliver the precision – in both target tracking and dose delivery – needed to confidently increase dose per fraction. Facing pressure to maximize practice efficiency to protect economic outcomes, clinicians also recognize that conventional tools are an inadequate solution. Finally, to deliver comfortable, high-quality patient experiences, clinicians recognize the need to move away from constrictive patient immobilization and breath-hold techniques. To rise to the challenges of the age of value-based care, RT teams need precision that doesn't come at the expense of versatility, efficiency or patient comfort – treating every patient and every indication with the highest degree of accuracy.

Meeting New Standards

Motion compensation techniques which: a) sacrifice margins, requiring expansive ITVs; b) move the target to the beam, requiring gating, breath holding or repositioning the patient; or c) attempt to stop the movement, requiring constraining devices or breath holding, frustrate practitioners. Common motion compensation techniques are not optimal for a value-based, mainstream, hypofractionated treatment landscape. In spite of this, technologies exist today that enable true, real-time motion tracking, treatment delivery adaptation, and beam synchronization – enabling dramatic improvements over traditional motion compensation:

1. MORE EFFICIENT: Gating typically has a duty cycle of less than 30%, meaning the beam is only on during the small faction of time when the target is in the treatment window.[1] This is inherently inefficient. The efficiency of breath holding depends on the capabilities of the patient, and pausing to re-position the patient is the most time-consuming. By contrast, true real-time motion tracking and beam synchronization enables 100% beam-on times throughout the target's motion – achieving the maximum potential efficiencies of hypofractionated RT.

2. MORE PRECISE:

For targets that move unpredictably: Put simply, because conventional treatment delivery platforms lack the mechanical capabilities to move the treatment beam to the target while delivering dose, most clinicians have been forced to use larger margins or to fix the patient or part of the patient's anatomy rigidly to prevent movement. Some conventional systems can track movement in real-time through implanted markers, but without the capability to react to the movement, treatment has to pause and then resume – or be stopped entirely until the patient is repositioned. Motion synchronization systems have developed anatomy and indication-specific motion tracking algorithms that don't require patient restraints. Intra-fraction imaging provides tracking of the target so that delivery synchronization can occur, maintaining sub-millimeter accuracy with a 100% beam-on time.[2]

For cyclically moving targets: While breath holding, using compression to limit the range of motion, or restraining the patient may minimize movement in some cases, practitioners recognize that some movement will still occur. Therefore ITVs (larger margins) must remain in the plan. In addition, even the most careful plan that accounts for breathing motion observed pre-treatment can be wrong on the day of treatment. But breathing patterns change – typically changing both from day to day, and often changing during treatment as patients relax during treatment. Therefore, pre-treatment positioning often does not match actual target positioning during treatment. Motion synchronization systems utilize fully integrated imaging and real-time, intelligent motion modeling to constantly re-evaluate and adjust the respiratory model to drive accurate and precise treatment delivery. This real-time tracking, treatment delivery adaptation, and beam synchronization enables precision in delivery synchronization but with a 100% beam-on time that dramatically speeds delivery times.[2]

3. BETTER PATIENT EXPERIENCES: Not surprisingly, the "move the patient to the beam" approach fails the "patient-first" test. Immobilization techniques cause significant discomfort, and even frequent repositioning can be frustrating. Breath holding just asks the patient to behave unnaturally over and over, while many patients are not capable of holding their breath because of their condition. Real-time motion tracking and beam synchronization gives the patient much greater freedom to relax and act naturally.

[1] *Jiang S B, Technical aspects of image-guided respiration-gated radiation therapy. Med Dosim. 2006; 31: 141-51.*
[2] *Eric Schnarr, Matt Beneke, Dylan Casey, Edward Chao, Jonathan Chappelow, Andrea Cox, Doug Henderson, Petr Jordan, Etienne Lessard, Dan Lucas, Andriy Myronenko, and Calvin Maurer, Feasibility of real-time motion management with helical tomotherapy Med. Phys. 45 (4), April 2018 Medical Physics published by Wiley periodicals, Inc. on behalf of American Association of Physicists in Medicine.*

ACCURAY

Building Radiation Therapy Platforms For the Age Of Value-based Care

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Throughout the history of Accuray, our legacy of innovation has been defined by our ability to adapt to meet the evolving needs of the field of radiation oncology. Moreover, our history is defined by a constant re-definition of accuracy, precision and versatility in radiotherapy. Our approach enables clinicians to treat any patient, with any indication, without compromising treatment quality or patient experience – while simultaneously providing practices with required clinical and financial results to survive and thrive both today and in the ever-changing tomorrow. Now, we are leveraging our entire legacy of innovation to capture the full potential of hypofractionated and ultra-hypofractionated RT.

The CyberKnife® System gives clinicians the unprecedented accuracy of the world's first and only radiotherapy robot. Building on the unique capabilities of the CyberKnife robot to move the treatment beam to any position to deliver non-coplanar, or non-isocentric treatment, we developed unique motion-tracking algorithms that stand unparalleled in the industry and allow the system to perform artificial intelligence (AI) driven treatment delivery adaptation and beam synchronization when targets move. Originally utilized as an SRS device, the CyberKnife System can now treat indications anywhere in the body with a range of fractionation schedules. Recent advances in planning, optimization and delivery allow treatment plans to be created and delivered in times similar to, or less than, conventional radiation treatment systems – even for targets that move.

The Radixact® Treatment Delivery System builds on the world's first truly helical radiotherapy delivery platform – leveraging a unique, continuously rotating gantry to enable highly conformal dose delivery. Leveraging more than a decade of leading expertise in motion management, we have adapted proven CyberKnife motion-tracking algorithms to drive the Radixact System's new motion synchronization & real-time adaptation* capabilities. Radixact's high-speed multileaf collimator (MLC) – dramatically faster than anything in the industry – combined with dynamic jaws enables high-speed beam-shaping to provide real-time adaptive delivery and motion synchronization. We have built a transformative innovation on the foundation of proven technologies – a system that offers the powerful accuracy and precision of AI driven real-time motion synchronization, with the reliable "workhorse" versatility of a helical delivery platform.

No clinician wants to spend time thinking about whether the radiation therapy system they are using can deliver their target clinical and financial outcomes. Today, Accuray is proud to offer versatile, worry-free and future-proof solutions: next-generation treatment delivery platforms ready to perform today, tomorrow, and in the future of value-based care.

*Synchrony, on the Radixact System, is an optional upgrade available for purchase.