

Medical Policy



Title: Real-Time Intrafraction Motion Management During Radiotherapy

Professional

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DESCRIPTION

This policy discusses the use of real-time intra-fraction target tracking during radiation therapy ("real-time tracking"). These techniques enable adjustment of the target radiation while it is being delivered (i.e., intra-fraction adjustments) to compensate for movement of the organ inside the body. Real-time tracking, which may or may not use radiographic images, is one of many techniques referred to as image-guided radiation therapy (IGRT). For this policy, real-time tracking is defined as frequent or continuous target tracking in the treatment room during radiotherapy, with periodic or continuous adjustment to targeting made on the basis of target motion detected by the tracking system. This policy does not address approaches used to optimize consistency of patient positioning in setting up either the overall treatment plan or individual treatment sessions (i.e., intrafraction adjustments); instead it deals with approaches to

monitor target movement within a single treatment session, which includes technologies using respiratory gating. This policy does not address IGRT used as part of stereotactic (body) radiotherapy.

Background

In general, intrafraction adjustments can be grouped into 2 categories: online and offline. An online correction takes place when corrections or actions occur at the time of radiation delivery on the basis of predefined thresholds. An offline approach refers to target tracking without immediate intervention.

During radiotherapy, it is important to target the tumor so that radiation treatment is delivered to the tumor, but surrounding tissue is spared. This targeting seems increasingly important as dose-escalation is used in an attempt to improve long-term tumor control and improve patient survival. Over time, a number of approaches have evolved to improve targeting of the radiation dose. Better targeting has been achieved through various approaches to radiation therapy, such as 3-dimensional conformal treatment (3D-CRT) and intensity-modulated radiation therapy (IMRT). For prostate cancer, use of a rectal balloon has been reported to improve consistent positioning of the prostate and thus reduce rectal tissue irradiation during radiotherapy treatment of prostate cancer. In addition, more sophisticated imaging techniques, including use of implanted fiducial (radio-opaque) markers, has been used to better position the tumor (patient) as part of treatment planning and individual radiation treatment sessions.

Intrafraction target motion can be caused by many things including breathing, cardiac and bowel motion, swallowing or sneezing. Data also suggest that a strong relationship may exist between obesity and organ shift, indicating that without some form of target tracking, the target volume may not receive the intended dose for patients who are moderately to severely obese.² Respiration affects the position of all thoracic and abdominal organs, primarily the lungs, liver, and breast.³ The American Association of Physicists in Medicine Task Group 76 recommends motion management for tumor motion that exceeds 5 mm in any direction or if significant normal tissue-sparing can be gained.⁴ Measurement of tumor motion commonly uses fluoroscopy or 4-dimensional computed tomography (4D-CT), a sequence of 3D-CT images over time, with or without fiducial markers.

Five principal respiratory motion management techniques are commonly used: integration of respiratory movements (i.e., mean tumor position, range of motion) into treatment planning; abdominal compression plates to force shallow breathing; breath-hold, often using spirometry; respiratory gating; and real-time tumor-tracking.⁵ Respiratory gating delivers radiation during a particular portion of the breathing cycle. This "gate" is defined by monitoring respiratory motion with external sensors and selecting a constant cycle amplitude or phase (e.g., end-inspiration or end-expiration) for radiation delivery. Respiratory gating assumes a consistent association between the respiratory cycle and tumor position. For patients in whom this association is unreliable, real-time target tracking techniques can be used. These techniques involve fluoroscopic, radiograph, or digital tracking of external respiratory surrogates, egg, an abdominal belt, or, like other real-time tumor-tracking techniques described here, implanted fiducial markers.⁶

As previously noted, the next step in this evolving process of improved targeting is the use of devices to track the target (tumor motion) during radiation treatment sessions and allow

adjustment of the radiation dose during a session based on tumor movement. Some of the devices cleared by FDA are referred to as "4-D imaging" (not to be confused with 4D-CT, described earlier). One such device is the Calypso® 4D Localization System (Varian Medical Systems, Palo Alto, CA). This system uses a group of 3 electromagnetic transponders (Beacon®) implanted in or near the tumor to allow continuous localization of a treatment isocenter. Beacon® transponders are 8.5-mm long and have a diameter of 1.85 mm. The 3 transponders have a "field of view" of 14-cm square with a depth of 27 cm.

REGULATORY STATUS

The Calypso® 4D Localization System obtained FDA clearance for prostate cancer in March 2006 through the 510(k) process (K060906) and for other soft tissue tumors in May 2008 (K080726). This system was considered equivalent to existing devices such as implanted fiducials and other body-positioning technologies.

Respiratory-gating systems by several manufacturers have received FDA approval, e.g., Real-time Position Management□ (RPM; Varian Medical Systems, Palo Alto, CA; K102024), Active Breathing Coordinator System® (ABC; Aktina Medical, Congers, NY; K003330), and SDX® (Dyn'R, Toulouse, France; K092479).

This policy does not address IGRT used as part of stereotactic (body) radiotherapy.

POLICY

- A. Real-time intrafraction target tracking during radiotherapy to adjust radiation doses or monitor target movement during individual radiotherapy treatment sessions is considered **experimental / investigational**.
- B. Respiratory gating techniques for the delivery of radiotherapy are considered **experimental / investigational**.

Policy Guidelines

This policy only addresses real-time tracking and devices defined as devices that allow for the adjustment of radiation doses during individual radiation treatment sessions.

RATIONALE

This policy was updated with searches of the MEDLINE database. The most recent literature review was performed on April 21, 2014. Following is a summary of the key literature to date.

Randomized trial data are needed to show the impact on clinical outcomes of real-time tracking devices that allow for adjustments during radiotherapy or monitor the tumor target during individual treatment sessions. The clinical outcomes could be disease control (patient survival) and/or toxicity (e.g., less damage to adjacent normal tissue). Because intensity-modulated radiotherapy (IMRT) and IMRT plus real-time tracking are likely to produce equivalent therapeutic results, given the increased cost of real-time tracking, the technique (tracking) needs to demonstrate incremental clinical benefit over IMRT. To date, clinical outcome studies have not been reported for any tumor site but are required to show that target tracking during radiotherapy leads to a clinically meaningful change in outcomes. Most work in this evolving area is in prostate cancer, although there also are studies in other organs such as lung, breast, and bladder.

Studies have focused on movement of the target during radiotherapy sessions. This is considered an initial step in evaluating this technology but not sufficient to determine if patient outcomes are improved. As observed by Dawson and Jaffray in 2007, clinically meaningful thresholds for target tracking and replanning of treatment during a course of radiotherapy are as yet unknown.⁷ Even less is known about impacts on outcomes of target tracking within a single treatment session.

These new devices appear to provide accurate localization. In 2008, Santanam et al reported on the localization accuracy of electromagnetic tracking systems and on-board imaging systems.⁸ In this study, both the imaging system and the electromagnetic system showed submillimeter accuracy during a study of both a phantom and a canine model. Kindblom et al (2009) similarly showed electromagnetic tracking was feasible with the Micropos transponder system (Micropos Medical, Göteborg, Sweden) and that the accuracy of transponder localization was comparable to radiograph localization of radiopaque markers.⁹ Smith et al (2009) successfully coupled an electromagnetic tracking system with linear accelerator gating for lung cancer.¹⁰ A currently registered trial that was determining movement of the cervix during radiotherapy has been withdrawn (NCT00907634).

Movement

Prostate Cancer

In a 2007 clinical study, Kupelian et al described differences found in radiotherapy sessions performed on 35 patients with prostate cancer.¹¹ In this article, 6 of the initial 41 patients could not be studied because body habitus (AP dimension) was too large to allow imaging. The results showed good agreement with radiograph localization. Displacements of 3 mm or more and 5 mm or more for cumulative duration of at least 30 seconds were observed during 41% and 15% of radiation sessions, respectively. The clinical sites for the study developed individualized protocols for responding to observed intrafraction motion. This publication did not report on clinical implications or clinical outcomes, either for control of disease or treatment complications (e.g., proctitis). The clinical impact of these displacements and resultant adjustments in treatments need to be explored in much greater detail.

In a 2008 retrospective analysis of data collected from the treatment of 21 patients with prostate cancer treated with CyberKnife (Accuray, Sunnyvale, CA), Xie et al reported on intrafractional movement of the prostate during hypofractionated radiotherapy.¹² The analysis included 427 datasets comprising movement deviations within an acceptable level (≈ 5 mm). The mean duration of intervals during which the prostate remained within 5 mm of its planned position was approximately 697 seconds. At 30 seconds, motion of more than 2 mm was present in approximately 5% of datasets. The percentage increased to 8%, 11%, and 14% at 60, 90, and 120 seconds, respectively. The authors concluded that these movements could be easily managed with a combination of manual couch movements and adjustment by the robotic arm. As noted earlier, the clinical impact of these displacements and resultant adjustments in treatments needs to be explored in much greater detail.

Langen et al (2008) reported on 17 patients treated at one of the centers in the study noted in the preceding paragraph.¹³ In this study, overall, the prostate was displaced by more than 3 mm in 13.6% of treatment time and by more than 5 mm in 3.3% of treatment time. Results for median (instead of mean) treatment time were 10.5% and 2.0%, respectively. Again, the clinical impact of this movement was not determined. The authors commented that potential clinical impact would depend on a number of factors including the clinical target volume. In this small series, intrafraction movement did not change to a large degree during treatment. However, the likelihood of displacement increased as time elapsed after positioning.

In 2009, Noel et al published data showing that intermittent target tracking is more sensitive than pre- and posttreatment target tracking to assess intrafraction prostate motion, but to reach sufficient sensitivity, intermittent imaging must be performed at a high sampling rate.¹⁴ They concluded that this supports the value of continuous real-time tracking. While this may be true, there is a major gap in the literature addressing the actual consequences of organ motion during radiotherapy. Li et al (2008) analyzed data from 1267 tracking sessions from 35 patients to look at the dosimetric consequences on intrafraction organ motion during radiotherapy.¹⁵ Results showed that even for the patients showing the largest overall movement, the prostate uniform equivalent dose was reduced by only 0.23%, and the minimum prostate dose remained over 95% of the nominal dose. When margins of 2 mm were used, the equivalent uniform dose was reduced by 0.51%, but sparing of the rectum and bladder was significantly reduced using the smaller margins. This study did not report on clinical outcomes, and data from a larger randomized cohort will be needed to verify these results.

Three prospective cohort studies assessed the impact of real-time intrafraction target tracking on planning target volume (PTV) margins. Tanyi et al (2010)¹⁶ and Curtis et al (2012)¹⁷ both used the Calypso® system in men with prostate cancer undergoing IMRT (total N=45). Each patient had 3 transponders implanted in the prostate gland. To deliver 95% of the prescribed dose to 95% of the clinical target volume in 90% of patients, margin requirements with intrafraction target tracking ranged from 1.4 mm in the lateral direction to 2.3 mm in the vertical direction. Without intrafraction target tracking, required margins were 2.1 mm and 10.5 mm, respectively, using bony alignment, and 2.8 mm and 3.2 mm, respectively, using image-guided marker alignment.¹⁶ Curtis et al (2013) found that without intrafraction adjustments, PTV margins of 5 mm were needed to ensure complete geometric coverage.¹⁷ With image-guided adjustments every 4 minutes, margins could be reduced to 3 mm. In the third study, Langsenlehner et al (2013) enrolled 44 men with prostate cancer undergoing 3-dimensional conformal radiotherapy (3D-CRT).¹⁸ PTV margins could be reduced from 2.6 mm in the lateral direction and 9.6 mm in the vertical direction using bony alignment, to 2.5 mm and 4.6 mm, respectively, using alignment to 4 implanted gold fiducial markers. None of these studies reported survival or morbidity outcomes associated with margin reductions.

In the 2013 Langsenlehner et al study just described,¹⁸ the authors noted that PTV margins could be reduced even further (to 2.4 mm laterally and 3.9 mm vertically) if treatment time was reduced to 4 minutes or less. This finding was confirmed by Cramer et al in their 2013 study of 143 men with localized prostate cancer who were undergoing conventional IMRT (47%) or faster intensity-modulated arc therapy (IMAT) (53%).¹⁹ Continuous (10 Hz) intrafraction motion tracking was used in all patients. Positions of implanted electromagnetic transponders were validated at least weekly by volumetric cone-beam computed tomography (CBCT). For each treatment technique evaluated (i.e., IMRT vs IMAT and setups based on electromagnetic transponders only vs electromagnetic transponders plus CBCT verification), prostate motion increased progressively as a function of elapsed treatment session duration (IMRT with CBCT verification longest).

Lung Cancer

In 2013, Shah et al reported an observational study of the Calypso® system in 7 patients with non-small-cell lung cancer (NSCLC).²⁰ The purpose of the study was to assess the feasibility of transponder implantation and data acquisition; motion-tracking data were not used to alter radiation treatment. Beacon® transponders and fiducial markers (used to fix transponders in place) were placed bronchoscopically in all patients. However, implantation was "difficult and unreliable for routine clinical use," e.g., due to pneumothorax in 1 patient and transponder migration during implantation. Similarly, motion tracking was possible but "required additional techniques not practical in a clinical setting," e.g., use of surface transponders to bypass limitations of the Calypso® system, such as a requirement for at least 2 transponders to initiate tracking.

Breast Cancer

A 2012 systematic review reported on inter- and intrafraction motion during whole-breast irradiation in the supine position.²¹ Literature search was conducted in November 2011, and 18 articles met inclusion criteria. Seven studies (total N=73 patients, >10,000 images) reported on intrafraction motion. Pooled motion variation was approximately 2 mm in several dimensions (left-right [lateral], anteroposterior [vertical], craniocaudal [longitudinal]), indicating that *intrafraction* motion may have larger effects on radiation dosing. However, because intrafraction

motion also was small (<5 mm), the authors suggested that PTV margins of 5 mm may be acceptable. A 2012 study of whole-breast irradiation in the supine position (N=23) aligned with this result.²² Li et al outlined the breast using radio-opaque wires on the skin (optical surface-guided whole-breast irradiation). Mean (SD) intrafraction motion was 0.1 mm (2.8) in the horizontal and 0.0 mm (2.2) in the longitudinal domain. Given the small amount of intrafraction motion detected in these studies, real-time intrafraction tracking may be unnecessary in unselected patients with breast cancer.

Morbidity

Sandler et al (2010) reported on 64 patients treated with IMRT for prostate cancer in the Assessing the Impact of Margin Reduction (AIM) study.²³ Patients were implanted with Beacon® transponders and were treated with IMRT to a nominal dose of 81 Gy in 1.8 Gy fractions. Patients in this study were treated with reduced tumor margins and real-time target tracking. Patient-reported morbidity associated with radiotherapy was the primary outcome. Study participants were compared with 153 unmatched historical controls; study participants had less favorable clinical characteristics than the comparator patients. Study participants reported fewer treatment-related symptoms and/or worsening of symptoms after treatment than the comparison group. For example, the proportion of patients in the historical comparison group reporting rectal urgency increased from 3% pretreatment to 22% posttreatment; no such increase was observed in the experimental group.

Disease Control/Patient Survival

Prostate Cancer

A 2013 review of image-guided radiotherapy technologies for prostate cancer acknowledged the lack of clinical trials demonstrating improved clinical outcomes with Calypso® 4D.²⁴

Bladder Cancer

Nishioka et al (2014) developed a prototype real-time target tracking system in Japan.²⁵ Using the system, this group conducted a prospective study of 20 patients with clinically inoperable (or surgery refused), stage II/III (node-negative) urothelial bladder carcinoma. All patients had undergone transurethral tumor resection followed by 40 Gy whole-bladder irradiation and implantation of fiducial markers. This was followed by a 25 Gy boost using the prototype target tracking system. Fourteen patients (70%) with adequate renal function (creatinine clearance, ≥ 45 mL/min) received concurrent chemoradiotherapy with nedaplatin, a second-generation platinum complex with reduced gastrointestinal and renal toxicity. Patients were followed every 3 months with cystoscopy and urine cytology; median follow-up was 56 months (range, 9-126). Acute grade 3 toxicities were urinary tract infections in 2 patients and thrombocytopenia in 1 patient; none were attributed to implantation of fiducial markers. Late treatment-related, grade 3 toxicities were hemorrhagic cystitis and intestinal obstruction due to adhesions in 1 patient each. Estimated 5-year local control rate (defined as absence of pathologically proven recurrence in the bladder) and overall survival were 64% and 61%, respectively. These results support further investigation in larger controlled studies.

Other Cancers

There are few registered clinical trials of these techniques, and none of a randomized design focused on showing how these additional procedures may improve clinical outcomes, including a decrease in toxicity to surrounding tissue.

Respiratory Gating

Because current nongated radiotherapy techniques achieve adequate tumor coverage, the goal of adding respiratory gating is to reduce irradiation of normal tissue to reduce toxicity and facilitate dose escalation.¹

Lung Cancer

Two small studies compared respiratory-gated and nongated treatment plans in patients with thoracic tumors. Vlachaki et al (2009) evaluated 10 patients (8 with NSCLC, 1 with small cell lung cancer [SCLC], and 1 undetermined due to risk of pneumothorax associated with biopsy) who were treated at several U.S. centers.²⁶ All patients underwent gated and nongated radiotherapy treatment planning using 4D-conformal treatment (4D-CT). PTV was determined by adding a 1.5 cm or 0.5 cm margin to the clinical target volume in nongated and gated plans, respectively. In each patient, PTVs were smaller in gated compared with nongated plans (mean PTV, 293 mL vs 575 mL, $p < 0.001$), which was attributed to the smaller (0.5 cm) margin used in gated plans. Mean and maximum PTV doses were similar in both plans, but minimum dose was higher in gated plans (53 Gy vs 48 Gy). Mean percentage of total lung volume (outside the PTV) exposed to 20 Gy or more of radiation (lung V20) was 26% in gated and 35% in nongated plans ($p < 0.001$). Mean doses to the heart and esophagus also were lower with gated versus nongated plans (11 Gy and 17 Gy vs 16 Gy and 22 Gy, respectively; $p \leq 0.003$).

In 2013, Hau et al evaluated 34 consecutive patients who were treated for thoracic malignancy (23 [68%] NSCLC, 10 [29%] SCLC, 1 [3%] atypical carcinoid) at a single center in Australia.¹ All patients underwent radiotherapy treatment planning using both a respiratory-gated approach and a free-breathing (nongated) approach. In both plans, a 5.5-mm margin was added to the clinical target volume to derive PTV margins. For respiratory-gated radiotherapy, PTV was selected to cover any tumor motion within the gating window. For the free-breathing approach, PTV was determined to encompass tumor throughout the respiratory cycle. PTV was smaller in respiratory-gated compared with nongated plans (388 cm³ vs 421 cm³, $p < 0.001$), but 95% uniform dose coverage was similar between the 2 plans (94% vs 96%, $p = 0.028$). Bonferroni correction for multiple comparisons yielded a p value less than 0.003 for statistical significance. A priori, a minimum 5% reduction in lung V20 was considered clinically significant. Mean (SD) lung V20 was 23% (9) in gated plans and 25% (9) in nongated plans, for a difference of 2 percentage points (95% confidence interval, 1 to 3; $p < 0.001$). Dosimetric data indicated no statistical difference in radiation doses to the spinal cord, heart, or esophagus. Four patients (12%) had lung V20 reductions of 5% or greater; 75% of these patients had superior-inferior tumor displacement of more than 1 cm compared with 2 (7%) of 30 patients whose lung V20 reduction did not exceed 5% (Fisher exact test, $p < 0.006$). The 4 patients also tended to have gross tumor volumes less than 100 cm³. Based on these observations, the authors suggested that respiratory gating be applied selectively to patients with gross tumor volumes less than 100 cm³ and superior-inferior tumor displacement of more than 1 cm.

Breast Cancer

A 2011 prospective, nonrandomized study by the French Ministry of Health compared respiratory-gated radiotherapy with standard conformal radiotherapy.^{27,28} Women (N=401) from 20 centers in France who had early stage breast cancer requiring radiotherapy only were enrolled. In the respiratory-gated group (n=218 [54%]), PTV margins were determined by computed tomography (CT) images of radio-opaque surface markers encircling the breast. For most patients in this group (93%), a spirometric breath-holding system was used for gating; 15

patients were gated by a real-time respiratory tracking system that used surface markers. In the standard conformal group (n=183 [46%]), PTV margins were determined by adding 10 mm to the clinical target volume. PTVs were statistically smaller in the respiratory-gated group compared with the standard conformal group (p<0.001). Total radiation dose did not differ statistically between groups. Dosimetric data indicated statistically greater radiation doses to the lungs, heart, and esophagus (organs at risk) in the standard conformal group. This benefit was attributed to the deep inspiration breath-hold respiratory gating technique because these patients had markedly increased total lung volumes, and therefore reduced normal lung tissue irradiated compared with patients treated with real-time tracking. Acute pulmonary toxicity (all grades) occurred in 48% of the standard conformal group and 36% of the respiratory-gated group (p=0.02). This difference persisted until the 12-month assessment. Other acute toxicities did not differ between groups in severity or type (e.g., cutaneous, esophageal, cardiac). Late esophageal toxicity (all grades) occurred at 6 months in 6% of the standard conformal group and 3% of the respiratory-gated group, but no longer differed between groups at 12 or 24 months. Other late toxicities did not differ between groups. After a median follow-up of 26 months (range, 1-47), there was no difference between groups in overall survival or disease-free survival.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might impact this policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
<i>Prostate cancer</i>			
NCT02033343	Phase I Feasibility Study of Prostate Cancer Radiotherapy Using Realtime Dynamic Multileaf Collimator Adaptation and Radiofrequency Tracking (Calypso)	30	Dec 2018
NCT01588938	External Immobilization Compared to Limited Immobilization Using a Novel Real-time Localization System of the Prostate	20	Sep 2016
NCT01624623	Post-prostatectomy Daily Target Guided Radiotherapy Using Real-Time, State of the Art Motion Tracking With Calypso 4D Localization System: A Feasibility Study	20	Aug 2016
NCT01589939	Reduced PTV Margins for the Treatment of Prostate Cancer with IMRT Using Real-Time, State-of-the- Art Motion Tracking With the Calypso 4D Localization System: A Feasibility	40	Sep 2016
<i>Lung cancer</i>			
NCT02111681	Calypso-based Deep Inspiration Breath Hold (DIBH) Radiation Treatments of Lung Cancer	30	Apr 2016
NCT01396551	Evaluating an Anchored Transponder in Lung Cancer Patients Receiving Radiation Therapy	70	Dec 2016
Unpublished			
<i>Prostate cancer</i>			
NCT00980993	Pilot Study on the Quantification of Respiratory-Induced Prostate Motion During Radiation Therapy Using Continuous Real-time Tracking	5	Sep 2010

NCT: national clinical trial.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through 3 academic medical centers and 1 physician specialty society (3 reviewers) when this policy was under review in 2014. Clinical input on the use of real-time intrafraction target tracking was mixed. Some respondents supported medical necessity for tumors subject to intrafraction motion, e.g., lung and breast; others did not. Three of 5 respondents agreed that head to head trials with and without the use of real-time target tracking are necessary to determine whether the use of real-time tracking leads to improved outcomes.

Summary of Evidence

Real-Time Intrafraction Target Tracking

Evidence for the use of real-time intrafraction target tracking for delivery of radiotherapy comprises studies, mostly in patients with prostate cancer, that demonstrate the ability of the technology to track tumor motion. Planning studies indicate that planning target volumes can be reduced with real-time intrafraction target tracking compared with usual setups (e.g., bony alignment). One study in patients with lung cancer reported difficulties with implantation of radio-emitting transponders, and 1 study in patients with breast cancer indicated little use for real-time intrafraction target tracking because breast tumor motion was small.

Because real-time intrafraction target tracking generally uses intensity-modulated radiotherapy (IMRT) to deliver radiotherapy, the use of real-time tracking is unlikely to produce outcomes that are inferior to IMRT treatment. Thus, on this basis, the real-time tracking approach is not considered to be investigational.

However, there are no data indicating that use of real-time tracking during radiotherapy to adjust the intrafraction dose of radiotherapy or monitor target motion during radiation treatment improves clinical outcomes over existing techniques. Clinical input was mixed, with several reviewers agreeing that head-to-head comparative trials with and without the use of real-time target tracking are necessary to determine whether the use of real-time tracking leads to improved outcomes. Because current evidence is insufficient to demonstrate health benefits, real-time intrafraction target tracking is considered investigational.

Respiratory Gating

Current nongated radiotherapy techniques achieve adequate tumor coverage. Therefore, the goal of adding respiratory gating is to reduce irradiation of normal tissue to reduce toxicity and facilitate dose escalation.¹ Increased treatment time and patient inconvenience associated with respiratory gating may be offset if these benefits are realized.

Studies in lung cancer and breast cancer have compared radiation treatment planning with and without respiratory gating using surface markers. Although studies have shown reductions in planning target volume margins, radiation doses to other organs at risk (lungs, heart, esophagus), and local toxicity with respiratory gating, these studies were small and the largest

study, in women with breast cancer, was nonrandomized. Increased survival or recurrence outcomes were not shown. Current evidence is therefore considered insufficient to determine whether respiratory gating improves patient outcomes, specifically by reducing toxicity and/or improving survival outcomes. Respiratory gating techniques for the delivery of radiotherapy are considered investigational.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Prostate Cancer

Current National Comprehensive Cancer Network (NCCN) clinical practice guidelines for prostate cancer (v.1.2015) state, "The accuracy of treatment should be improved by attention to daily prostate localization, with techniques of IGRT [image-guided radiotherapy] using CT [computed tomography], ultrasound, implanted fiducials, electromagnetic targeting/tracking, or an endorectal balloon to improve oncologic cure rates and reduce side effects."²⁹ NCCN has replaced "daily IGRT with 3D-CRT [conformal radiotherapy]/IMRT" with "highly conformal" or 3D-CRT/IMRT throughout the guidelines. Highly conformal radiotherapy techniques should be used to treat prostate cancer. For primary external beam radiotherapy, IGRT is required if the dose is 78 Gy or more. NCCN is applying a broader definition of IGRT and is addressing intrafraction (daily) adjustment rather than intrafraction adjustments, which are the focus of this policy. Although NCCN states that unless otherwise noted, all recommendations are based on level 2A evidence, no specific citations are provided for their conclusions.

Lung Cancer

Current NCCN guidelines for non-small-cell lung cancer (v.5.2015)³⁰ and small cell lung cancer (v.1.2015)³¹ state, "Respiratory motion should be managed when motion is excessive." Recommended approaches include beam-gating with the respiratory cycle and dynamic tumor tracking. When motion is minimal or the internal target volume is small, "motion-encompassing targeting" is appropriate.

Breast Cancer

Current NCCN guidelines for breast cancer (v.2.2015) state that the goals of radiotherapy are "uniform dose distribution and minimal normal tissue toxicity."³² Respiratory gating is one of several strategies recommended to accomplish these goals (along with prone positioning and use of wedges, IMRT, and/or forward planning using segments). A recommendation for real-time target tracking is not included.

Bladder Cancer

Current NCCN guidelines for bladder cancer (v.1.2015) do not include a recommendation for real-time intrafraction target tracking in patients receiving radiotherapy.³³

American College of Radiology

American College of Radiology appropriateness criteria for radiotherapy in prostate cancer,³⁴ cervical cancer,^{35,36} and non-small-cell lung cancer^{37,38} do not include ratings for real-time intrafraction target tracking.

American Urological Association

A 2013 guideline issued jointly by the American Urological Association and the American Society for Radiation Oncology addressed adjuvant and salvage radiotherapy after prostatectomy. This guideline did not include real-time intrafraction target tracking.³⁹

National Institute for Health and Care Excellence

A 2014 National Institute for Health and Care Excellence guideline on the diagnosis and treatment of prostate cancer did not include a recommendation for real-time intrafraction target tracking during radiotherapy.⁴⁰

U.S. Preventive Services Task Force Recommendations

Not applicable.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

32553	Placement of interstitial device(s) for radiation therapy guidance (e.g., fiducial markers, dosimeter), percutaneous, intra-thoracic, single or multiple
49411	Placement of interstitial device(s) for radiation therapy guidance (e.g., fiducial markers, dosimeter), percutaneous, intra-abdominal, intra-pelvic (except prostate), and/or retroperitoneum, single or multiple
55876	Placement of interstitial device(s) for radiation therapy guidance (e.g., fiducial markers, dosimeter), prostate (via needle, any approach), single or multiple
77385	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking , when performed; simple
77386	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking , when performed; complex
77387	Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
A4648	Tissue marker, implantable, any type, each
A4649	Surgical supply; miscellaneous
A4650	Implantable radiation dosimeter, each
C9728	Placement of interstitial devices(s) for radiation therapy/surgery guidance (e.g., fiducial markers, dosimeter), for other than the following sites (any approach): abdomen, pelvis, prostate, retroperitoneum, thorax, single or multiple)
G6017	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

- Effective in 2015, CPT code 0197T (Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface

tracking), each fraction of treatment) was deleted and new coding for intrafraction tracking was created: 77385, 77386, 77387.

- The Centers for Medicare and Medicaid Services (CMS) decided not to implement this change for 2015 and instead created HCPCS G codes for the radiation therapy codes being deleted 12/31/14. So the following code may be used for this localization: G6017.
- Between 2009 and 2015, there was a specific CPT category III code for this localization: 0197T.
- Prior to 2015, CPT code 77421 (stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy) may have been incorrectly reported for this intra-fraction tracking procedure.
- There are no codes specific to the Beacon transponders. The implantation of the transponders can be coded using CPT codes, such as 32553, 49411, and 55876, based on the anatomical location. Code C9728 is also available for assignment.
- The supply of the device is reported separately. The transponders would most likely be coded using A4648, but might also be coded using A4650, or an unlisted code such as A4649.

ICD-10 DIAGNOSIS

Experimental / investigational for all diagnoses related to this policy.

REVISIONS

03-10-2011	Policy added to the bcbsks.com web site.
03-19-2013	Description section updated
	In Coding section: <ul style="list-style-type: none"> ▪ Added CPT codes: 32553, 49411 ▪ Updated Coding notations
	Rationale section updated
	References updated
01-01-2015	In Coding section: <ul style="list-style-type: none"> ▪ Added CPT/ HCPCS Codes: 77385, 77386, 77387, G6017 (Effective January 1, 2015) ▪ Deleted CPT Code: 0197T (Effective January 1, 2015) ▪ Added HCPCS Code: C9728 (correction to coding section)
01-01-2017	Policy published 12-01-2016. Policy effective 01-01-2017.
	Title revised from "Real-Time Intrafraction Target Tracking During Radiation Therapy" to "Real-Time Intrafraction Motion Management During Radiotherapy"
	Description section updated
	In Policy section: <ul style="list-style-type: none"> ▪ In Item A revised "radiation therapy" to "radiotherapy" ▪ Added Item B "Respiratory gating techniques for the delivery of radiotherapy are considered experimental / investigational."
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> ▪ Revised Coding Notations ▪ In Diagnoses section added "or experimental / investigational" to read "Not medically necessary or experimental / investigational for all diagnoses related to this policy."
	References updated
03-01-2019	Policy published 01-30-2019. Policy effective 03-01-2019.
	Policy reviewed with no changes made to Description, Rationale or References.
	In Policy section: <ul style="list-style-type: none"> ▪ In Item A removed "not medically necessary" and added "experimental / investigational" to read "Real-time intrafraction target tracking during radiotherapy to adjust radiation

	doses or monitor target movement during individual radiotherapy treatment sessions is considered experimental / investigational."
	In Coding Section: <ul style="list-style-type: none"> ▪ Revised nomenclature on CPT Code: 77387
02-24-2021	Medical Policy was reviewed with no revisions added.

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