Title: Real-Time Intra-Fraction Target Tracking during Radiation Therapy

**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 radiation therapy, 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., inter-fraction adjustments), instead it deals with approaches to monitor...
target movement within a single treatment session. This policy will also not address technologies using respiratory gating.

**Background**

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

During radiation therapy, 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-D conformal treatment 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 radiation therapy treatment of prostate cancer. In addition, more sophisticated imaging techniques, including use of implanted fiducial markers, has been used to better position the tumor (patient) as part of treatment planning and individual radiation treatment sessions.

Intra-fraction 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. (1)

As noted above, 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 the U.S. Food and Drug Administration (FDA) are referred to as “4-D imaging.” One such device is the Calypso® 4D Localization System. This system uses a group of 3 electromagnetic transponders (Beacon®) implanted in the prostate to allow continuous localization of a treatment isocenter. The 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.

The Calypso 4D Localization System obtained FDA clearance for prostate cancer in March 2006 through the 510(k) process (K060906). This system was considered equivalent to existing devices such as implanted fiducials.

This policy does not address IGRT used as part of stereotactic (body) radiation therapy.
P O L I C Y
Real-time intra-fraction target tracking during radiation therapy to adjust radiation doses or monitor target movement during individual radiation therapy treatment sessions is considered **not medically necessary**.

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.

R A T I O N A L E
This policy was originally created in 2008 and was updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period of December 1, 2011 through December 10, 2012. 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 radiation therapy 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). Since intensity-modulated radiation therapy (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 will be required to show that target tracking during radiotherapy leads to a clinically meaningful change in outcomes. The majority of the work in this evolving area is in prostate cancer, although there are also studies of the technique in other organs such as lung and breast.

Studies have focused on movement of the target during radiation therapy sessions. This is considered an initial step in evaluating this technology but is not sufficient to determine if patient outcomes are improved. As Dawson and Jaffray comment, the clinically meaningful thresholds for target tracking and re-planning of treatment during a course of radiation therapy are not yet known. (2) Even less is known about the impact of target tracking within a single treatment session.

These new devices do appear to provide accurate localization. Santanam and colleagues reported on the localization accuracy of electromagnetic tracking systems and on-board imaging systems. (3) 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. similarly showed electromagnetic tracking was feasible with the Micropos transponder system and that the accuracy of transponder localization was comparable to x-ray localization of radiopaque markers. (4) Smith et al. successfully coupled an electromagnetic tracking system with linear accelerator gating for lung cancer. (5) A currently registered trial is looking at the movement of the cervix during radiation therapy.

Literature Review
In a retrospective analysis of data collected from the treatment of 21 patients with prostate cancer treated with Cyberknife, Xie et al. reported on the intra-fractional movement of the
prostate during hypofractionated radiotherapy. The analysis included 427 datasets composed of the time it took for the prostate to move beyond an acceptable level (approximately 5 mm). The data suggest that it takes approximately 697 seconds for the prostate to move beyond 5 mm relative to its planned position and that motion of greater than 2 mm at 30 seconds was present in approximately 5% of datasets. The percentage increases to 8%, 11%, and 14% at 60, 90, and 120 seconds, respectively. They 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.

Noel et al. published data showing that intermittent target tracking is more sensitive than pre- and post-treatment target tracking to assess intra-fraction prostate motion, but to reach sufficient sensitivity, intermittent imaging must be performed at a high sampling rate. 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 radiation therapy. Li and colleagues analyzed data from 1,267 tracking sessions from 35 patients to look at the dosimetric consequences on intra-fraction organ motion during radiation therapy. 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.

Sandler and colleagues reported on 64 patients treated with IMRT for prostate cancer in the Assessing the Impact of Margin Reduction (AIM) study. Patients were implanted with Beacon transponders (Calypso Medical Technologies, Inc., Seattle, WA) 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, as well as real-time tumor tracking. Patient-reported morbidity associated with radiotherapy was the primary outcome. Study participants were compared to historic controls. Study participants reported fewer treatment-related symptoms and/or worsening of symptoms after treatment than the comparison group. For example, the percentage of patients in the historic comparison group reporting rectal urgency increased from 3% pre-treatment to 22% post-treatment, no increase was observed in the current experimental group.

In a clinical study, Kupelian et al. described differences found in radiation therapy sessions performed on 35 patients with prostate cancer. In this paper, 6 of the initial 41 patients could not be studied because body habitus (A-P dimension) was too large to allow imaging. The results showed good agreement with x-ray 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 intra-fraction 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 needs to be explored in much greater detail.

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

No relevant outcome studies have been published in the literature for any site including, but not limited to, prostate, lung, and breast. Additionally, there are few registered clinical trials of these techniques at this time, 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.

**Summary**

Because real-time intra-fraction target tracking generally uses IMRT to deliver radiation therapy, 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 that indicate that use of real-time tracking during radiation therapy to adjust the intra-fraction dose of radiation therapy or monitor target motion during radiation treatment improves clinical outcomes over existing techniques. In summary, because this technology is more costly than alternative services that produce equivalent therapeutic results, this is considered not medically necessary.

**Practice Guidelines and Position Statements**

The 2013 National Comprehensive Cancer Network (NCCN) clinical practice guidelines for prostate cancer state “The accuracy of treatment should be improved by attention to daily prostate localization, with techniques of IGRT [image-guided radiation therapy] using CT[computed tomography], ultrasound implanted fiducials, electromagnetic targeting/tracking, or an endorectal balloon to improve oncologic cure rates and reduce side effects.” (12) NCCN has replaced 3D-CRT (conformal radiotherapy)/IMRT with daily IGRT with IMRT/3D-CRT throughout the guidelines. For primary EBRT; IGRT is required if the dose is ≥78Gy. NCCN is applying a broader definition of IGRT and is addressing inter-fraction (daily) adjustment rather than intra-fraction 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 basis of their conclusions.
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 (eg, fiducial markers, dosimeter), percutaneous, intra-thoracic, single or multiple
49411   Placement of interstitial device(s) for radiation therapy guidance (eg, 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 (eg, fiducial markers, dosimeter), prostate (via needle, any approach), single or multiple
0197T   Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (eg, 3D positional tracking, gating, 3D surface tracking), each fraction of treatment
A4648   Tissue marker, implantable, any type, each
A4649   Surgical supply; miscellaneous
A4650   Implantable radiation dosimeter, each

- Effective in 2009, there is a specific CPT category III code for this localization: 0197T.
- 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
- 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.
- CPT code 77421 – stereoscopic X-ray guidance for localization of target volume for the delivery of radiation therapy – may be incorrectly reported for this intra-fraction tracking procedure.

DIAGNOSIS

Not medically necessary for all diagnoses related to this policy.

REVISIONS

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<tr>
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REFERENCES