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Image-Guided Radiotherapy: Has It Influenced Patient Outcomes?

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Cancer control and toxicity outcomes are the mainstay of evidence-based medicine in radiation oncology. However, radiotherapy is an intricate therapy involving numerous processes that need to be executed appropriately in order for the therapy to be delivered successfully. The use of image-guided radiation therapy (IGRT), referring to imaging occurring in the radiation therapy room with per-patient adjustments, can increase the agreement between the planned and the actual dose delivered. However, the absence of direct evidence regarding the clinical benefit of IGRT has been a criticism. Here, we dissect the role of IGRT in the radiotherapy (RT) process and emphasize its role in improving the quality of the intervention. The literature is reviewed to collect evidence that supports that higher-quality dose delivery enabled by IGRT results in higher clinical control rates, reduced toxicity, and new treatment options for patients that previously were without viable options.

Radiotherapy (RT) is a proven means to improve survival, control tumor progression, address symptoms, and improve the quality of life of cancer patients across the globe. This is achieved through the delivery of high-quality treatment that includes geometrically accurate conformal deposition of ionizing radiation and best efforts to spare the neighboring radiosensitive healthy tissues. The path to high-quality RT is complex but can be decomposed into steps, from timely diagnosis, then accurate staging and clinical assessment, appropriate choice of radiation dose and volume to be irradiated, and radiation delivery to the intended target volume with reliable quality (ie, minimal difference in prescribed treatment vs delivered). Finally, a thorough evaluation of many clinical endpoints is required to evaluate the benefit of radiation therapy in an individual patient and in a population of patients so that an action can be taken for a specific diagnosis (Fig 1A). As in any complex process, uncertainties exist in each of these steps, and the field has been transformed as new technologies allow greater conformality of dose to the target, increasing the concern of failures at other, weaker components of the process. A major factor affecting the quality of treatment arises from geometric uncertainties in the placement of dose within the body over the course of RT. Image-guided radiation therapy (IGRT), defined as imaging in the treatment room, with positional adjustments for geometric deviations, represents an advanced quality assurance tool for successful radiation therapy. Given the capital and manpower costs of this technology, it is reasonable to examine the evidence that supports this quality assurance activity.

Although it may be difficult to directly evaluate the limited evidence for IGRT, it is possible to examine improved clinical outcomes that have been enabled by IGRT. For example, in the absence of a direct impact on clinical outcomes, can IGRT eliminate variance and reduce the chance of a large geometric miss? In other words, what is the consequence of not performing it? Success rates in general vary widely (Fig 1B). To be able to reduce one source of uncertainty (ie, less geometric and dosimetric variance with IGRT) may help increase the chance of successful patient outcomes.

Therefore, we have identified 3 questions to be examined in this review: (1) Is there evidence to support the hypothesis that the quality improvements associated with IGRT improve clinical control rates? (2) Is there evidence to support the hypothesis that the appropriate use of IGRT can reduce toxicity? and (3) Are there new RT treatments being enabled because of the higher quality of RT that can be delivered with IGRT technology? There is no prospective randomized trial on IGRT technologies, nor is there ever likely to be one given the role that technology plays as a critical component of quality assurance. The consenting of patients to 2 arms of an intervention in which 2 different levels of

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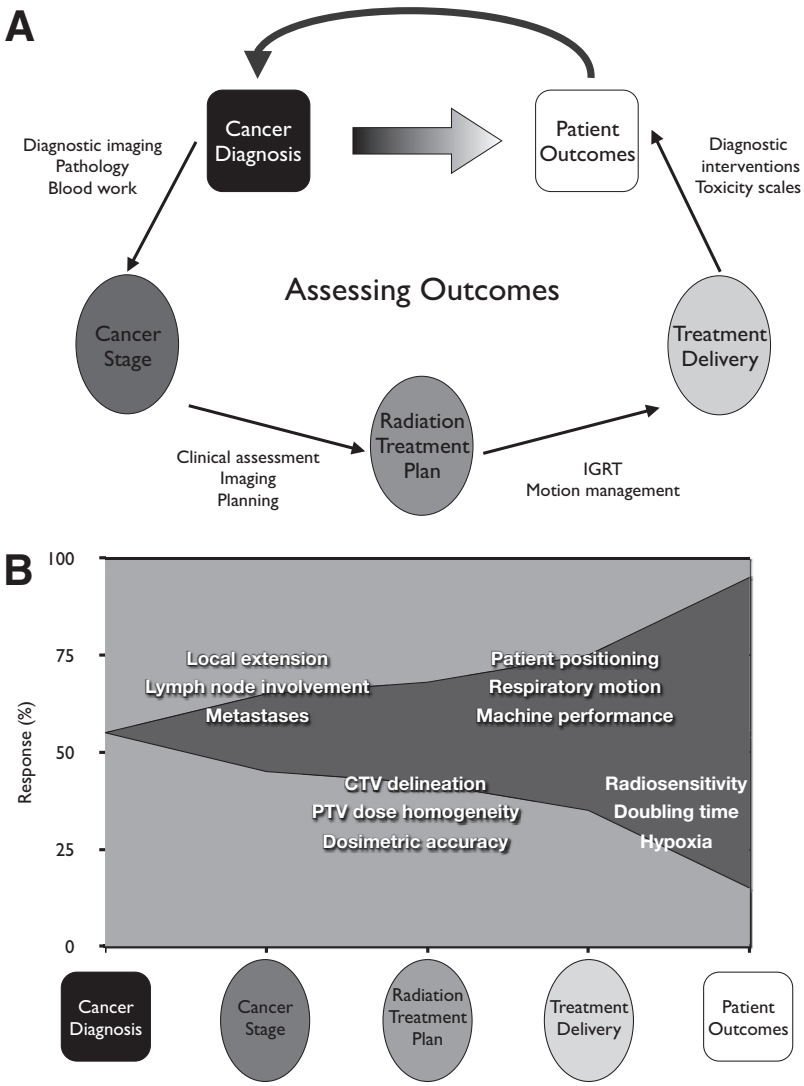

Figure 1 Cancer treatment and outcomes measurement involves multiple steps. (A) To go from cancer diagnosis to patient outcomes, interventions are in fact required to go from 1 step to the other; each passage is associated with a level of error. (B) An example of a hypothetical outcome associated with a given cancer diagnosis. However, only the end result, or range of outcomes, is known. It is the consequence of the multiplication of errors from each step. Two conclusions may be drawn: the final error bar is large and every attempt at reducing it is worthwhile and the impact of any single intervention is small by itself.

quality assurance are used would be challenging. However, the evidence may accumulate through different practices in different populations that use different methods of varying quality because of other factors, such as cost, availability, training, and so on. Given the lack of prospective data, the questions described earlier have been examined through a retrospective review of the literature. Before describing the analysis, an overview of IGRT, its role in ensuring the quality of radiation delivery, and the challenges associated with isolating IGRT as a treatment technique within the framework of RT are presented.

Quality and IGRT

IGRT Implementation and the Tools of Quality

There is a notable increase in the number of radiation oncology publications referencing or using quality management and statistical process control tools.[1-14] Interest in these tools has been motivated by the desire to improve the safety of radiation therapy as well as recognition that they may allow improvements in efficiency, standardization, and precision. Although there are many guidelines for the quality assurance of IGRT equipment,[15-17] there are few that specifically highlight the role of "IGRT as quality assurance"[18] or the potential of IGRT to reduce patient treatment incidents.[19]

As an example, patient positioning can be considered as a process, representing a series of tasks, with daily patient position as an output produced with variations in quality and daily online imaging as a quality control tool intended to reduce this variation. IGRT and the serial measurements of patient positioning that it produces are well matched to the quality tools of statistical process control. IGRT concepts, such as offline correction protocols[20,21] or adaptive RT processes,[22-24] can be seen as attempts to intervene on the varia-

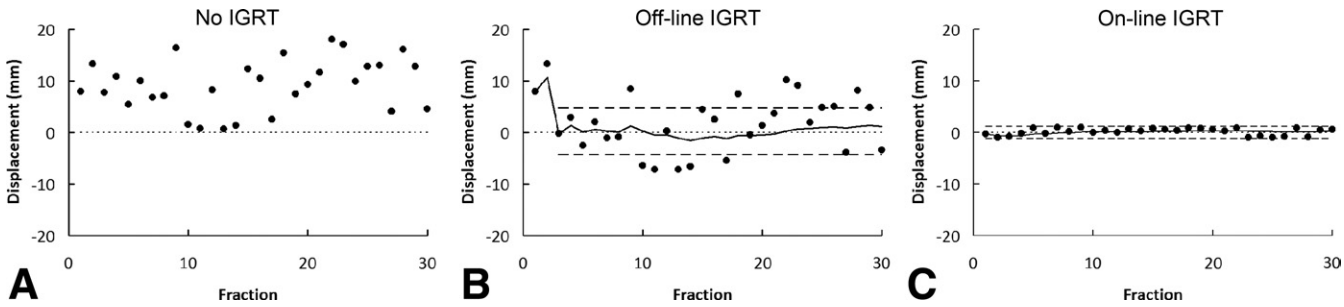

Figure 2 "Runtime" charts for the position of a single patient showing daily position (circles), running mean (solid line), and control limits (dashed lines). (A) The daily position without image guidance shows a large systematic error (10 mm) and large random uncertainty. (B) The application of an off-line correction protocol results in small systematic error but does not reduce large random uncertainties, which manifests as daily positions that are "out of control." (C) Using daily online corrections results in small systematic and random uncertainties, apparent as a process that is "in control."

tion shown on a process control chart. In the example in Figure 2, a shrinking action level off-line correction protocol can improve the treatment quality by efficiently reducing systematic error (note systematic error is corrected on the third fraction in this example). However, the off-line approach is not a daily quality control activity, and the result is a small systematic error with large residual daily random uncertainty shown by daily positions that are outside the control limits ("out of control"). A daily online correction protocol (eg, daily corrections for any deviation exceeding 1 mm before treatment in the Fig 2 example) results in a process with small systematic and random uncertainties and is "in control."

Impact of IGRT on Radiotherapy Quality

There are numerous publications that show that IGRT is an effective quality control process that reduces the variation (systematic and random uncertainties) in the output (patient position) of the process.[25-34] Computer simulations of these uncertainties suggest that their reduction could impact clinical endpoints.[35-39] IGRT also facilitates the detection and management of exceptional deviations, including emergent or spurious changes, such as gross positioning errors, weight loss, substantial organ deformations, systematic changes in internal organs, changes in respiratory motion, and so on.

Although a sense of equipoise does not appear to motivate clinical trials of IGRT, these technologies clearly allow improvements in the quality of clinical trials pursuing other questions in radiation therapy. Notably, many new high-quality radiation therapy clinical trials require the credentialing and routine use of IGRT. For example, almost all new Radiation Therapy Oncology Group trials for lung, head and neck, paraspinal, liver, sarcoma, and brain cancers require IGRT credentialing. By reducing geometric variability, variability in delivered dose is reduced, and, presumably, variation in clinical response can be expected to be decreased as well. This can be seen as "shrinking the cone" in Figure 1B. This reduced variance in a study endpoint increases the power of the study to detect statistically significant differences (eg, from a radiation sensitizer).

How IGRT May Impact Patient Outcomes

Correction of Systematic and Random Errors

IGRT increases the chance of RT being applied as planned so the intended doses are delivered to the targets. This process has been embedded in RT for many decades, and, as such, inferential arguments in favor of IGRT are numerous. Unforeseen differences between what is planned and what is delivered, in terms of radiation dose and volume, are to be avoided. These differences encompass small systematic errors up to frank misadministrations. In such an intricate treatment as RT, it is often not clear what the weakest link in the process is; patient selection, target identification, contouring variability, planning details, patient positioning, and motion management may all have a significant impact on dose deposition accuracy. In a treatment spanning a large number of fractions, the impact of execution variation, or random error, is usually less important than systematic errors.[40-42] However, if the number of fractions is reduced, then random error can also have a larger negative impact.[41] Other aspects to consider in the RT process are the immobilization of the patient and target and the accuracy of the registration surrogate used for IGRT (eg, larynx for early laryngeal cancer and whole liver for liver cancer). Planning target volume (PTV) margin recipes have been developed to take into account uncertainty related to these geometric uncertainties for a population, and IGRT is a tool that can measure geometric uncertainties that then can be fed into PTV margin recipes at each institution (ie, IGRT provides the means to measure geometrical offsets and develop more accurate PTV margins). Reduced PTV margins may reduce the risk of toxicity, whereas increased margins based on evidence may increase the chance of tumor control. In general, PTV margins will be reduced as more IGRT is used in clinics for the same chance

Table 1 Added Dose and Time per Modality per Fraction in Pelvis IGRT[44,158-161]

Modality	Dose at Midbody (cGy)	Time (min)*	Available Examples&
Ultrasound	0	2-3	BATCAM, Clarity
Plain kV†	0.1-0.6	0.1-3	Cyberknife, ExacTrac
Plain MV†	1-10	0.1-3	Various EPID and portal devices
kV CBCT‡	2-3	2-4	ARTISTE, OBI, XVI
MV CBCT	5-15	2-3	MVision
kV FBCT§	0.8-2.8	15	CTVision, EXaCT
MV FBCT	1.5-3	2-3	Tomotherapy

FBCT, fan-beam computed tomography scanning.
*Excludes image interpretation and action on observations.
&BATCAM™, Best nomos, Pittsburgh, PA; Clarity™ and XVI, Elekta, Stockholm, Sweden; Cyberknife™ and Tomotherapy™, Accuray, Sunnyvale, CA; EXaCT™, ExacTrac™ and OBI™, Varian Medical Systems, Inc., Palo Alto, CA; ARTISTE™, CTVision™ and MVision™, Siemens AG, Erlangen, Germany.
†For 2 incidences.
‡Full soft-tissue scan, 360°.
§Involves couch rotation and CT translation because CT scanning is not on linac gantry.

of tumor control compared with a non-IGRT era. A subsequent step is to examine how the change in PTV relates to differences in doses to both tumor targets and normal tissues to improve the therapeutic ratio.

IGRT is also used to detect individuals who may fall out of the predicted population-based margins. For example, patients with more variation in positioning who may have been inappropriately treated in the absence of IGRT may be detected in the era of IGRT.

Situations in Which IGRT May Not Be Recommended

As with any medical intervention, one must weigh the risk over the benefit. One of the potentially negative facets of IGRT is the extra radiation dose it involves.[43-45] Table 1 provides a list of the dose per fraction associated with a list of IGRT modalities. There is at least 1 report in which that dose was associated with more toxicity if not computed in the total dose delivered.[46] As low as reasonably achievable principles generally apply, and the technique and frequency of IGRT imaging should be adjusted based on the clinical goals. Soft-tissue targeting requires a higher-dose imaging technique, but high-contrast targets, such as bone or metallic fiducial markers, can be accurately visualized at imaging doses as low as 0.1 to 0.5 cGy. Careful selection of the extent of image acquisition can lower the dose even further. Also in Table 1 is the average extra time by IGRT technique for performing and assessing the images. Of note, there is additional time required for image interpretation and action on the results, which can be reduced with automatic evaluation tools and more experience. The overall time involved is a factor affecting whether to reduce or discard the use of IGRT in certain clinical situations. For example, a patient in acute pain being treated palliatively with a large safety margin may have his/her position verified with a relatively fast electronic portal image rather than a cone-beam computed tomography (CBCT) scan. Alternatively, an efficient process using fast, low-dose CBCT scanning to register to bone may be appropriate. Other boundaries in the appropriate use of IGRT are described in more detail below.

Clinical Examples Showing Benefit to IGRT

Radiosurgery and Hypofractionated Regimens

Central Nervous System

Radiosurgery for brain metastases improves local control and survival in appropriately selected patients.[47,48] Radiosurgery is also effective in a variety of other malignant and benign neurologic conditions. The landscape of brain radiosurgery has changed since the advent of IGRT, which has facilitated frameless radiosurgery. Frame elimination is less invasive, more comfortable for the patient, and potentially simpler for the care team, with regards to both resources and time. However, most clinical outcomes are based on historical non-IGRT series of patients treated with invasive rigid stereotactic frames. PTV margins of 0 to 3 mm are used in most centers with conflicting retrospective evidence of impact on local control or toxicity. Nataf et al[49] described a 12% increase in parenchymal toxicity by adding a 2-mm margin on the GTV, without improvement on local control. Conversely, Noël et al[50] found, after adding a 1-mm margin, an increase in the minimum dose to GTV, yielding a 39% absolute increase in local control without added toxicity. RTOG 90-05 escalated the dose to intracranial lesions and found an association between tumor size and neurotoxicity but not in lesion control. It is hypothesized that a larger spread of intermediate dose, a consequence of plans for larger tumors, could be responsible.[51] In summary, increased PTV margins can increase the neurologic tissues irradiated and increase the risk of neurotoxicity (which may range from subclinical to clinical neurological deficit); this motivates for the use of IGRT in this setting.

The impact of less rigid immobilization and potential dose blurring because of intrafraction motion is less clear. No direct clinical comparison exists, but 1 study by Ramakrishna et al[52] compared the geometric accuracy of a head frame to that of a thermoplastic mask with stereoscopic planar kV image guidance.[52] A reliable setup was used in both modali-

ties, but there was a concern over intrafraction motion for lesions smaller than 5 mm if no margin was added, given a 22% likelihood of a 1- to 2-mm shift without invasive immobilization. Given the other sources of uncertainty, larger tumors could then be treated with similar accuracy using both methods, and adding a margin of 1 to 2 mm could be considered otherwise. In support of this, retrospective series of frameless radiosurgery without a control group have shown control for brain metastases of 80% to 90%, which is similar to historical frame-based techniques.[53] However, toxicity has in general not yet been well described. Margins advocated vary between 0 and 3 mm with a variety of imaging modalities.[54-56]

Another advantage of IGRT comes from data for meningioma or benign neurologic disease patients. Fractionated, image-guided stereotactic radiotherapy did not compromise toxicity nor local control while treating patients with larger average target volumes and targets closer to critical structures compared with radiosurgery series with rigid invasive immobilization.[57,58] The different IGRT modalities have not been compared between themselves so far.

The evolution of spine radiosurgery parallels that of cranial treatments but with close to complete migration to noninvasive techniques along with reliable immobilization and imaging to ensure submillimeter accuracy and adequate dose distributions.[55,59-63] The gain for IGRT to avoid invasive immobilization is more obvious than in cranial radiosurgery to avoid the extensive surgical procedure required for the invasive fixation. Again, the nature of the evidence, variable fractionation schemes, and techniques confound the comparisons of outcomes. Most patients treated with spine stereotactic body radiotherapy (SBRT) are not curable, and avoidance of acute toxicity, especially to aerodigestive tract, is a goal in standard palliative fractionated RT as well as SBRT. Current SBRT outcomes, at least with regards to toxicity, are reassuring, and the ability to spare surrounding normal tissues is appealing, but the quality of life data is still pending.[64-66] Of interest, reirradiation to a significant dose allowed with SBRT has consistently yielded local and/or pain control above 90%. The figures expected with conventional reirradiation are in the the 35% to 85% range, but no direct comparison exists.[67] In summary, IGRT has facilitated the use of radiosurgery and spinal SBRT. Reduced PTVs with IGRT should reduce the risk of toxicity and improve the quality of life in these patients.

Lung and Liver SBRT

Respiration-induced motion and daily changes in the baseline tumor position of thoracic and upper abdomen targets have required the implementation of IGRT to make hypofractionated stereotactic treatments to those sites possible. The positive impact, although nonrandomized, of lung SBRT on local control and survival has put it forth, at least for stage I tumors, as a challenger of surgery.[68] However, even with a near-rigid fixation, such as a body frame or abdominal compression, a supplementary margin of up to 1.5 cm may be needed without further imaging to take into account differences between planned thoracic tumor position and real position at the time of treatment.[69,70] Even with breathing motion control techniques, setup uncertainties remain because substantial shifts in tumor position relative to the chest wall or vertebral bodies can be seen. With less intense immobilization (eg, arm cradles or vacuum cushions), some patients have an even larger systematic error in excess of 3 cm.[71,72] Combined with intrafraction breathing motion, this can lead to underdosage of the tumor of 15% or more.[73-75] The dose response of primary lung cancer, although with variable thresholds, has been established,[68] and a dose response for both primary and metastatic liver disease has been described.[76] Large PTV margins have the potential to increase toxicity, especially in patients with limited liver or lung parenchymal reserve. Thresholds of mean lung and mean liver doses have been associated with worse toxicity in SBRT.[77-79] With lung SBRT, bronchial toxicity, almost never seen in conventionally fractionated regimens, has been observed.[78] Luminal gastrointestinal toxicity is also important to consider in liver and other upper abdomen SBRT.[80] A reduction in PTV margins, facilitated with IGRT, can reduce the doses to such serial functioning normal tissues. Volumetric IGRT can be exploited by overlying isodoses from the treatment planning system on the daily patient images to help exclude sensitive structures from undue dose, especially if anatomy changes rapidly as is the case with gastrointestinal filling (Fig 3).

With lung and liver SBRT, data support an improvement in the required PTV margin and dose distribution from a variety of IGRT techniques.[25,29,34,81-91] Because IGRT allows a better understanding of the uncertainty involved at the outset if IGRT were not used, it is highly unlikely that protocols without in-treatment/online imaging and registration will be used in the future. To the contrary, the trend is rather toward an intensification of imaging to further reduce treatment margins (eg, with tracking techniques).

Summary

IGRT has enabled new treatment options, including frameless central nervous system radiosurgery or fractionated stereotactic RT and spine, lung, and liver SBRT. Cerebral radionecrosis, bronchial necrosis, and liver dysfunction are serious potential toxicities that need to be considered in these ablative therapies, and smaller PTV margins can reduce their risk. Although there are no randomized trials, SBRT for primary lung cancer is associated with local control and survival rates that rival surgery. Randomized trials of lung and liver SBRT are planned.

Conventional Fractionated RT

Conventionally fractionated regimens are more forgiving than hypofractionated approaches because a single gross geometric miss may only result in a change of a few percent in the overall delivered dose. Further compounded by the heterogeneous radiosensitivity of individual cancers or tissues, inferior outcomes may thus escape our detection thresholds.[92] Systematic errors remain, however, and should be avoided in most clinical scenarios as shown later.

Prostate

As dose escalation for prostate cancer is pushed forward by evidence, the risk of systematic error has increased as the PTV

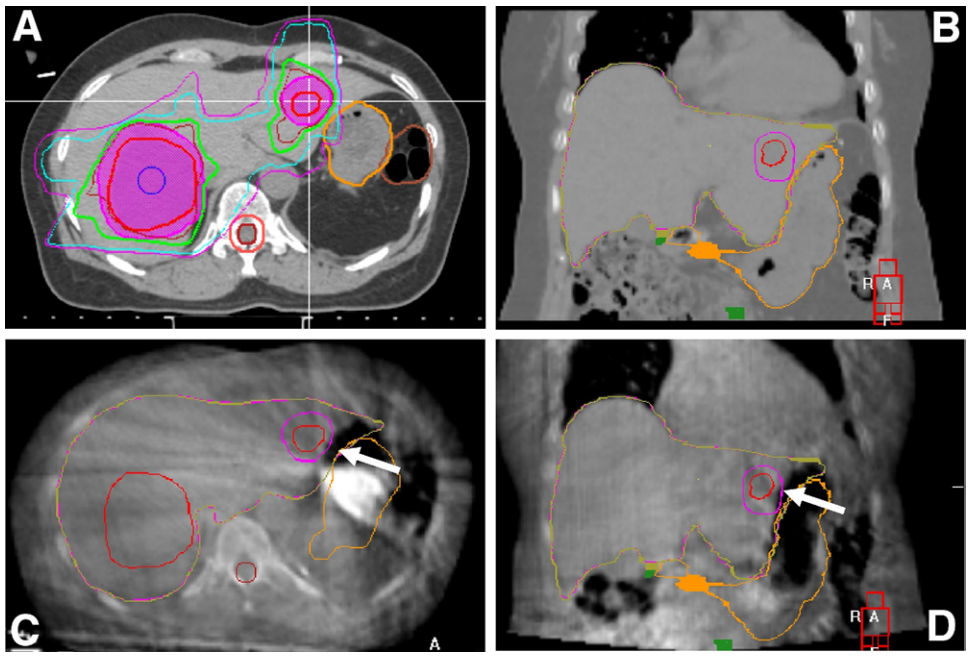

Figure 3 SBRT for metastases in left and right liver lobes. (A and B) Planning CT scans: 33 Gy (in 6 fractions) isodose line (green) is covering the PTVs (pink shadows) and avoiding the stomach (orange) on the planning CT. (C and D) Third-fraction CBCT scans: a random change in gastric filling (arrows), along with a small liver volume reduction, pushed the left lobe medially, whereas the right lobe alignment was acceptable. Without replanning the patient to account for the change, the dose to the stomach would have been higher than acceptable, and the left lobe tumor would potentially have been underdosed.

margins have decreased, especially with new techniques, such as IMRT and hypofractionation.[93-95] This has been shown in a retrospective analysis by de Crevoisier et al[96] and a secondary analysis of the Dutch dose escalation randomized trial by Heemsbergen et al.[97] They both found an absolute loss of close to 30% in biochemical control at 5 years if the rectum distention was above median at the time of planning. PTV margin was reduced, and IGRT consisted of bone matching using weekly electronic portal imaging device (EPID), with no prostate or fiducial based IGRT. It is postulated that the distended rectums at planning were not representative of the patient anatomy over the course of treatment because during therapy the rectum would likely empty and the prostate would move posteriorly outside of the high-dose region. In contrast, in a retrospective series of prostate patients treated with daily ultrasound-based prostate IGRT, different rectal fillings at planning were not related to outcomes even with a 4-mm PTV margin.[98] Another study by Engels et al[99] showed a significant difference of rectal cross-sectional area at planning on 5-year biochemical control, but this is overshadowed by the finding that the use of fiducial markers for prostate IGRT was negatively correlated with biochemical control. Of note, a smaller PTV and lower prescription dose was correlated with the use of fiducials, emphasizing how other sources of error are more likely to impact clinical outcomes as PTV margins are further reduced.

Margin size and dosimetric improvements from more stringent IGRT procedures are well documented.[37,100-111] Reductions in toxicity are also an important endpoint for a change in technique to be justified. An improvement in urinary and rectal toxicity has been described after a PTV reduction. This was corresponding to bladder and rectal DVH improvements and allowed by kV CBCT or fiducial markers for localization versus bone-matched EPID.[112,113]

Based on these facts, it is not surprising to find that skin tattoos and EPID with bone-matching perform equally poorly in predicting prostate localization.[114-116] In obese patients, because skin-based geometric uncertainties and motion are even larger, a 20% decrease in biochemical control has been described in the absence of prostate- or fiducial-based IGRT; of note, obesity itself may impact oncologic outcomes.[111,117] Overall, clinical comparisons of IGRT modalities or action level are still lacking.[118]

Head and Neck

The proximity of targets to critical structures in head and neck require high-dose gradients. Head and neck radiation techniques have then mandated more accuracy and reliability.[119-122] Again, it is a matter of "how much" rather than "if" IGRT is needed. Thermoplastic mask immobilization and weekly 2-dimensional imaging with bone matching was used with PTV margins of 5 mm for decades.[123] No direct impact of more intense IGRT has been shown, but a 50% reduction of PTV margins has been obtained when using daily CBCT scanning.[124,125] A note of caution is necessary in areas of the neck that are less well immobilized like the tongue, larynx, and lower neck.[126-128] A PTV reduction approach has been shown to be at least as safe with regards to local control in a

Figure 4 Man with squamous cell carcinoma and extensive atelectasis of the left lung. (A) Planning: PET-based gross tumor is in pink, and PTV is in red. (B) A bone-matched CBCT scan after 18 fractions: the lung has re-expanded, the hilar tumor (arrow) is now likely partly outside the PTV, breathing motion is increased, and the surrounding lung density has changed, all of which can lead to substantial underdosage in the absence of soft tissue IGRT. (Courtesy of Dr B. Fortin, Montreal, Canada.)

retrospective series comparing a margin of 5 mm versus 3 mm using daily volumetric IGRT.[129] A large dosimetric impact on parotid dose of daily volumetric imaging versus no correction was found by some[130] but not by others.[131] This contradiction is probably in part attributable to the good immobilization used in head and neck to reduce errors, and, in parallel with radiosurgery, a change in immobilization could help improve the patient's experience if the error is kept small by reliable IGRT.[132]

The ability of volumetric imaging to detect soft-tissue and tumor changes brings us to the brink of adaptive RT, which has the potential to improve outcomes, particularly in patients with bulky base of skull or paranasal sinus malignancies that abut critical normal tissues. So far, no clinical data have shown how much improvement adaptive RT may give or what the most appropriate action levels for replanning are.[133-135]

Other Sites

One of the first reports on the pertinence of in-treatment quality assessment comes from Hodgkin disease portal verification. Kinzie et al[136] attributed the higher relapse rate and marginal misses to failure to comply with the designed fields after the analysis of plain films. No direct clinical data are available for other sites, but an impact on margins and DVHs can be found for numerous anatomic sites.[137-139] In the case of conventional fractionation for lung tumors, individual patients with locally advanced lung cancer may benefit from the detection of significant tumor shrinkage, especially if it is associated with atelectasis at the time of planning (Fig 4). Although this affects a small proportion of patients, IGRT can be used to avoid a large systematic error in such patients.

Summary

An improvement in relapse rate in prostate cancer, Hodgkin disease, and head and neck cancers using IGRT has been consistently reported. IGRT is also used to identify anatomic modifications during treatment as part of a quality assurance program benefiting all cancer sites. There is a suggestion that prostate and head and neck cancer patients might have lower toxicity with IGRT, especially when combined with other technical advances like IMRT.

Brachytherapy

Image guidance has replaced geometric model–based brachytherapy prescription in most circumstances over the last 4 decades. Computed planning and 3D capability in the brachytherapy suite have recently been deemed essential to a state-of-the-art gynecology practice.[140]

Prostate

Initial brachytherapy techniques with permanent implants required direct visualization of the prostate at the time of surgery. Transrectal ultrasound was then introduced in preplanning and intraoperatively. The latter allowed direct visualization of needle placement inside the prostate and appropriate corrections if needed. It has improved not only the biochemical failure and the urinary toxicity rates but also seems to have allowed the elimination of the learning curve effect on dosimetric parameters usually observed with less experienced teams.[141-144] It has been shown that further accuracy, for example, with dynamic interactive dosimetry or immediate implant correction after seed position imaging can further improve the final dose distribution, but a true clinical impact is still uncertain.[145,146] Finally, these techniques have made possible prostate reirradiation with brachytherapy after primary external-beam failure as described in many contemporary series. Thus, IGRT has expanded the therapeutic options for these patients.[147]

Gynecologic

Orthogonal plain films for dose calculation and live ultrasound for optimal tandem positioning are accepted techniques,[140,148] but the use of 3D imaging from CT- or magnetic resonance–based gynecology brachytherapy planning addresses the dual purpose of volume delineation and assessment of the implant quality. The use of 3D imaging has shown that the dose to critical structures is significantly different from what was thought in the past but also that a better

representation of the observed toxicity and imaging can help to reduce these toxicities.[149-151] The historical comparison of local control rates has yielded impressive results as well.[152-154] Guidelines now exist to contour the rectum, bladder, and sigmoid as well as target volumes and prospective evaluation of the efficacy of 3D planning is under way.[155,156]

Summary

Brachytherapy local control and toxicity rates have both been improved through more extensive use of IGRT in prostate and gynecologic implants alike. The impact on the patient of the additional time required for imaging, contouring, and optimizing the treatment should also be evaluated in future studies that should also describe potential benefits in local control and toxicity.

Conclusions

In clinical practice, IGRT is currently a solid tool to tackle the problem of radiotherapy accuracy. State-of-the-art IGRT can reduce positioning uncertainty to the extent that a 1- to 2-mm PTV margin would often be sufficient to account for this uncertainty, especially if adequate immobilization and motion management are available. However, because of the other sources of error (including target delineation), the PTV margin for most RT treatments should be larger than 2 mm.[157] A rational mindset in implementing IGRT is to follow a "do no harm" approach. IGRT can be used as a quality assurance tool itself. IGRT has been shown to facilitate implementation of new RT techniques (eg, liver and lung SBRT) and in selected sites reduce toxicity and improve local control. An analysis of the geometric precision associated with a particular dosimetric advantage should be investigated. Then, the whole chain of interventions in the RT process should be prospectively assessed. This is particularly important because other steps in the RT process (eg, contouring or valid measurements of toxicity) are at least as important as high geometric precision.

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