Anniversary Paper: Role of medical physicists and the AAPM in improving geometric aspects of treatment accuracy and precision

Ellen D. Yorke
Medical Physics Department, Memorial Sloan-Kettering Cancer Center, New York, New York 10065

Paul Keall
Department of Radiation Oncology, Stanford University School of Medicine, Stanford, California 94305-5847

Frank Verhaegen
Medical Physics Unit, McGill University, Montreal, Quebec H3G 1A4, Canada

(Received 15 November 2007; revised 19 December 2007; accepted for publication 20 December 2007; published 12 February 2008)

The last 50 years have seen great advances in the accuracy of external beam radiation therapy. Geometrical uncertainties have been reduced from a centimeter or more in presimulation, skin-mark guided days to 1–2 mm in today’s image-guided radiation therapy treatments. Medical physicists, with the support and guidance of the American Association of Physicists in Medicine (AAPM), have been, and continue to be, at the forefront of research, development and clinical implementation in this area. This article reviews some of the major contributions of physicists to the improvement of treatment accuracy and precision, and speculates as to what the future may bring. © 2008 American Association of Physicists in Medicine, [DOI: 10.1118/1.2836420]

Key words: history of medical physics, treatment accuracy, target definition, patient setup, image guidance

I. INTRODUCTION

From the earliest days of radiation therapy, physicists have had major responsibility for quantifying and improving the precision and accuracy of radiation treatments. Physical dosimetry—determination of the absolute dose to water or tissue equivalent phantom material under tightly regulated conditions—was always recognized as the physicists’ realm and was perhaps the main reason for physics input to the field. Indeed, most of the therapy contributions to the first ten volumes of the journal Medical Physics dealt with physical dosimetry. But, it was obvious to those with clinical involvement that patients are not phantoms, that the treatment room is not a laboratory, and that it is important to know the location of tumor and normal tissues during planning and treatment.

1–5 Inaccurate initial localization of internal anatomy, voluntary and involuntary patient motion, therapy-induced time trends, natural tissue inhomogeneities, the difficulty of reproducibly positioning an often uncomfortable patient over a treatment course of several weeks, and the inevitability of human error in a stressful environment lead to uncertainties far greater than the ~2% attributed to dosimetry. 6–8 Reducing these effects is a highly interdisciplinary effort in which individual physicists and the American Association of Physicists in Medicine (AAPM) have been key players, as is demonstrated by the many familiar names and references to AAPM publications in the bibliography of this article. A number of recent reviews summarize current work, including Ref. 58 and the Image Guided Radiation Therapy (IGRT) portion of Ref. 9.

II. HISTORICAL BACKGROUND

II.A. “In the beginning”

Radiobiological studies, analysis of clinical outcomes for a range of planned doses, and the results of unintended clinical events documented in the mid 1960s and early 1970s provided evidence that systematic dose increases of approximately 10% could improve local control and/or increase normal tissue toxicity, while similar systematic decreases reduced local control. 10–13 Modeling by several physicists based on an assumed sigmoidal dose-response for tumor control probability (TCP) (Refs. 3, 7, 14, and 15) showed that small (3–5 mm) regions of underdose that can be caused by systematic positional uncertainties can drastically decrease TCP, while overly wide margins put normal tissue at risk of complications. 3,7 Thus, the need for accuracy in treatment was well appreciated. But, how to achieve it was more of a problem.

It is necessary for each patient’s target and risk organs to be well localized so that suitable field arrangements can be designed. Either these anatomical structures must remain within a few millimeters of their initial location for every day of a 4–6 week treatment course or their shifts must be measured and accounted for by treatment alterations. As a “back-to-the-future” note in these days of on-board imaging, the very first klystron-based linear accelerator built at Stanford and used clinically in 1956 had a fluoroscope mounted in line with the linac in which an x-ray tube could be moved to the linac position (Fig. 1). 16 Hammersmith Hospital in the UK in 1953 was the first to treat with a magnetron-based linac. And, in 1959, Johns and Cunningham described a diagnostic x-ray tube mounted on the head of a Co-60 therapy
unit to obtain good-quality images from the perspective of the therapy beam to use for both simulation and treatment verification. 

The conventional simulator, developed in the early 1960s, provided the advantages of a dedicated unit where diagnostic-quality radiographs, fluoroscopic images, and patient-specific geometric data could be obtained under conditions that mimicked treatment. Customized immobilization and repositioning aids could be constructed more conveniently at a dedicated machine that did not also have to maintain a treatment schedule. References 19 and 20 are both practical and historical reviews of treatment simulators.

Reproducible patient localization for treatment during the early years of radiation therapy was accomplished with the use of wall-mounted systems of focused projector lights and/or rigid mechanical back pointers and similar devices, often in conjunction with a fixed source-skin distance treatment technique. In one physicist’s recollection, “You bring back evil memories from a happily forgotten past when I spent my time playing with bubble levels and graph paper at 2:00 AM. Actually the original projector lights were optical components from modified bomb sights (I believe WW II), which were mounted to the walls and ceilings using aluminum plates that could be adjusted by screws.” (Richard Fleishman, personal communication). Some of these tools are shown and described in detail in the classic textbook *The Physics of Radiology* by Johns and Cunningham. A patent for the application of low-power lasers to patient alignment was awarded to Lescrenier and Sandberg in 1970, which the author learned during a telephone conversation with Mrs. Lescrenier. Lescrenier’s company, Gammex was founded in 1969 and continues to be the major vendor of alignment lasers. Lasers are more patient and user-friendly than mechanical rods and are much better suited to isocentric treatments.

Megavoltage port films, acquired regularly during the treatment course and compared with radiographs from simulation, were recognized as a convenient, practical way to monitor the positional constancy of bony anatomy and other structures with sufficient contrast. Although radiation therapists are most directly involved in immobilization and simulation, perceptive physicists recognized the importance of these processes to treatment outcomes. Simulators became increasingly common radiation oncology equipment and a 1985 Patterns of Care study found inferior clinical outcome in departments that lacked a conventional simulator.

Strict immobilization and very accurate target localization are particularly important for the tight dose distributions of proton therapy. Physicists associated with the proton therapy facility at the MGH/Harvard Cyclotron Laboratory that commenced treatment in 1961 were leaders in developing the philosophy and tools for improving geometric aspects of treatment across all external beam modalities.

During the 1970s, three new imaging tools were developed that led to dramatic improvements in patient-specific localization of both tumors and risk organs. These innovations were the result of cross-disciplinary work and physicists played major roles in these endeavors. The first hospital computed tomography (CT) scanners were installed in 1972 and an electrical engineer (Hounsfield) and a physicist ( Cormack), received the 1979 Nobel Prize in medicine for their independent, seminal contributions. Medical magnetic resonance imaging, based on the methods of nuclear magnetic resonance originally devised for atomic and materials physics, was developed during the same time period by a physical chemist (Lauterbur), a physicist (Mansfield), and a mathematically-inclined physician (Damadian). CT and MRI provided unparalleled noninvasive access to anatomic information. Further, the frontiers of “biological imaging” were opened to radiation therapy applications with the development of positron emission tomography (PET) by a team that included a physicist (Ter-Pogossian) and other physical scientists (Phelps and Hoffman). The full potential of MRI and PET in designing treatments and monitoring and evaluating radiation treatment accuracy has not yet been reached and we look forward to investigational work and research breakthroughs in applications of “molecular imaging” in years to come.

II.B. The 3D era

By the early 1980s, CT scanners were generally available in a diagnostic radiology setting. A number of single-institution studies in which physicists were vital participants demonstrated that target coverage was significantly improved by incorporating CT information into treatment planning. CT imaging also reinforced general consciousness that, as stated in a far-sighted article in *Medical Physics*, “cancer is a three-dimensional disease.”

It was awkward to interface diagnostic CT images acquired at one session with a conventional simulation performed at a different time (often in a different department or even hospital) for formal radiation therapy treatment plan-
ning. Accurate alignment lasers, use of a flat rather than curved couch, and software to implement particular radiation therapy-related requirements were needed to customize a CT scanner for radiation therapy planning applications. Further advantage was gained by staffing such CT scanners with people who understood the special demands of maintaining internal and external anatomic position set at simulation over the entire treatment course. Ref. 29 is a description of an early, in-house “CT-simulator.”

Within this same period, computer speed and memory had advanced to a point that allowed for three-dimensional (3D) anatomical visualization and volumetric dose calculations in a clinically reasonable time frame.32 Physicists23,33 developed the concept of beam’s eye view (BEV), which permits a user to perform a “virtual simulation”34 and to design apertures shaped to conform to a tumor. A major deficiency of CT simulation was the inability of acquiring CT images at the treatment machine for monitoring treatment setup reproducibility. While modern developments do allow for 3D imaging at the treatment unit, at the time the problem was solved by software to generate digitally reconstructed radiographs (DRRs) from the CT image set.35 DRRs could be windowed to mimic megavoltage radiographs and had the further advantage that CT-based contours of tumors or other structures not visible on physical radiographs could be projected onto a DRR. The improvements in target and risk organ localization and in volumetric dose calculation encouraged increasing use of patient-customized, conformal treatment plans with beam directions, apertures, and beam weights selected to give approximately uniform target coverage and superior normal tissue sparing. Although “2D” treatment plans with simple beam arrangements accounted for the majority of treatments, three-dimensional conformal radiation therapy—3D-CRT—moved strongly into the clinical arena. In 1984, the NCI funded the “Collaborative Working Group on the evaluation of treatment planning for external photon beam radiotherapy,” which brought together radiation oncologists and physicists from four institutions to study the potential provided by the new tools. This group produced several seminal reports published in Volume 21, No. 1 of the International Journal of Radiation Oncology, Biology, and Physics.

In fact, during the years of transition from 2D to 3D, most North American journal publications relating to physics input to improving the geometric accuracy of treatment appeared in journals other than Medical Physics, which tended to emphasize physical dosimetry, dose calculation in phantom, and hardware development. But, the concern of AAPM members with geometric treatment accuracy is clear in the Proceedings of the 1986 and 1990 AAPM Summer Schools. Contributions of particular relevance to this review are Refs. 7, 26, 32, and 36–38 in the 1986 Proceedings and Refs. 39–41 in the 1990 Proceedings.

To benefit from the conformal treatment plans, clinicians had to be sure that the plans were accurately implemented. This required careful review of megavoltage port films, preferably at least weekly over the course of treatment. Review was often difficult due to poor image quality and the awkward techniques required to register them with DRRs or radiographs acquired during a conventional simulation.142–44 Many physicists were leaders in the improvement of image quality and in the quantitative analyses that established typical magnitudes and distributions of setup errors at different disease sites and under different immobilization conditions. The extensive reference lists of Refs. 45–47 include many of these original contributions, reminding us that treatment protocols need be designed with setup errors in mind.48

A number of medical physicists, among them AAPM Charter Member Norman Baily, participated in developing and implementing the clinical use of electronic portal imaging devices (EPIDs).40–51 EPIDs allowed faster image acquisition and easier qualitative and quantitative comparison with reference images. Europe adopted this technology much more rapidly than North America,52,53 but the lag is now overcome as many clinics go wholly or at least partially filmless. By providing images faster and often at lower dose than film, and offering the user measurement and interactive registration capabilities that were previously impossible or very slow, EPIDs are a key component to the “IGRT” era whose rise coincides with the 50th anniversary of AAPM.

III. MANAGING UNCERTAINTIES IN THE RADIOTHERAPY PROCESS

III.A. Target and risk organ definition

An accurate three-dimensional model of the patient at simulation is a prerequisite for accurate radiation therapy. To build this model requires patient images on which the tumor and risk organs can be localized and delineated. Radiation oncologists and diagnostic radiologists bear the primary responsibility for this, but physicists take the lead in developing and improving imaging and computational tools that use the images and other information provided by the physician (e.g., “the contours”) to devise and deliver the treatment plan.

CT images dominate radiation therapy for many reasons. They are geometrically accurate, readily interpreted relative to normal anatomy, have a known relationship between the image intensity (CT number) and local electron density needed for accurate dose calculation, and can easily be processed to produce DRRs to compare with radiographs. Further, in comparison to MRI and nuclear imaging facilities, CT scanners and facilities are low cost with easy patient preparation and high patient throughput. These features are, in part, responsible for the rapid development of CT simulation. But, the superior soft tissue contrast of MRI images makes them particularly helpful in discriminating target and soft tissue critical structures for brain and prostate treatment planning.54–57 PET images provide biological information that is useful for fine-tuning target definition at some disease sites: for example, FDG-PET is increasingly used to assist target delineation for non-small-cell lung cancer. Some studies indicate that magnetic resonance spectroscopic imaging (MRSI) can detect areas of “aggressive” tumor and may be important in planning deliberately nonuniform target dose distributions.55,56,62
SPECT (Ref. 63) and functional MRI (Refs. 36, 54, 56, and 64) images may help plan normal tissue avoidance strategies in the thorax and brain, respectively. Thus, despite technical and practical challenges, structure definition on the planning CT scan is often supplemented by other imaging modalities.

In general, images from the planning CT and the other modalities are acquired with different setups, often with different patient positions on different days and in different departments. Physicists are particularly aware that combining the studies by visual inspection is highly subjective and dependent on individual skill, experience, and/or biases. Formal image registration methods for radiation therapy were developed in the early 1990s, and this remains a major research area that blurs the boundaries between therapy and diagnostic physicists and involves engineers and applied mathematicians as well. The earliest applications registered CT and MR studies in the brain, where rigid body transformations are adequate, providing geometric distortion of the MR image is corrected. Careful setup that duplicates simulation positioning for the other imaging procedures can partially compensate for nonrigid anatomy at other disease sites. But, accurate rigid registration may be prevented by incompatibility of the patient’s immobilization aids and the imaging machine or anatomical changes between the sessions. Deformable image registration methods are under active development; a search of PubMed for “deformable registration for radiation therapy” turned up 44 articles between 1/2001 and 9/2007.

For an imaging modality to assist accurate structure definition, it is necessary that the images be geometrically faithful or that deviations be quantitatively understood and correctable in software, and that overall image quality be maintained. Further, the treatment planning system must include tools for correct and accurate use of these images. A unique contribution of medical physicists is the design and implementation of strict quality assurance (QA) methods to verify the continuing integrity of the information provided by each imaging system, and to ensure that the treatment planning software and clinical personnel are capable of using it correctly. Throughout its history, the AAPM has given strong institutional support to the preparation and promulgation of guidance documents. Seventeen of the 99 reports available through the AAPM website deal with aspects of such QA, as do seven of the currently active task groups. Of particular note are cautions and tests of aspects of the treatment planning system related to the anatomic patient model described in the report of TG53 (Ref. 69) and in the ESTRO Physics Booklet 7.

Having an accurate 3D snapshot of patient anatomy is only the first step. Integrating this information into a systematic method that ensures accurate dose delivery is the subject of the next sections.

III.B. Reasons for deviations from the simulation model at treatment

There are four major systems in the body that cause motion on scales significant for radiotherapy: the muscular-skeletal, respiratory, gastrointestinal, and cardiac systems. Day-to-day changes in patient pose can be caused by misalignment of the patient in immobilization devices and of the external anatomy with respect to the treatment beam. Physiological changes affect the relative positions and shapes of internal anatomy, such as tumor growth or shrinkage, diet, rectal filling, and weight loss. The knowledge of the causes of temporal changes with time is not new. However, what has evolved over time are the tools to measure the magnitude of the changes that result in uncertainty in beam-tumor targeting, systems to rationally combine uncertainties, and tools to reduce the uncertainty induced by the anatomic changes.

III.B.1. Imaging development

The mainstay of managing uncertainties has been x-ray imaging. As described in Sec. II B, the clinical implementation of EPIDs for megavoltage imaging was an important development. And, decades after the very early efforts mentioned in the Introduction, the combination of an integrated kV x-ray imaging system (or systems) with the linear accelerator resurfaced in the 1990s.

Currently there are many other imaging techniques including ultrasound and the use of different parts of the electromagnetic spectrum. In addition to kV and MV imaging, optical imaging, electromagnetic (transponder and MR-based), and a variety of respiratory monitors are available or under development.

III.C. Formalizing margins

The International Commission on Radiation Units and Measurements (ICRU) compiled, in 1993, and updated in 1999, a framework for prescribing, reporting, and recording radiotherapy. Three key volumes were defined: the gross tumor volume (GTV), clinical target volume (CTV), and planning target volume (PTV). The concepts of including geometric uncertainty into treatment planning through the addition of margins between the CTV and PTV were described, though the formalism for margin addition was not specified, and several possibilities were proposed (e.g., summation or quadrature addition). Important residual uncertainties of the interobserver GTV delineation variations and the stochastic GTV-CTV margin (with sparse data) were discussed. In moving forward with ever-increasingly complex IGRT strategies, medical physicists and the treatment team need to be cognizant of the residual errors in the radiotherapy process.

A key development in the formalization of appropriate margins for radiotherapy was the separation of radiotherapy errors into systematic (causing a shift of the dose distribution to first order) and random (causing a blurring of the dose distribution to first order). This was first described by Stroom et al. and has been extended by several authors, most notably van Herk, whose excellent review on errors and margins is given in Ref. 73. The most widely used margin formula is that of van Herk, where the CTV to PTV margin,
III.D. Margin reduction strategies

Physicists are trained in quantitative thinking and are therefore the leaders in measuring the distributions of systematic and random setup errors for various patient populations and in designing rational and practical intervention strategies to reduce the uncertainties in both. References 45, 76, and 77 review some of the extensive literature in this area. The comprehensive quality assurance report of AAPM’s TG 40 (Ref. 78) recommended at least weekly review of treatment field radiographs as a guard against large errors. However, more protocols achieve further reductions in systematic error (Δ) and/or random error (σ), thereby reducing the volume of normal tissue irradiated to harmful doses by reducing the PTV. Technical developments, including those mentioned in this paper and Ref. 9, have improved the efficiency of these procedures and encouraged their clinical use beyond large academic centers.

Three classes of margin reduction strategies are currently in clinical use: online, offline, and adaptive.76 Online strategies localize the target or its surrogates before each treatment by comparing simulation data with radiographs,79,80 nonionizing radiation references,81 or most recently, three-dimensional imaging (in-room CT, tomoscopy imaging, and MV and kV cone-beam CT imaging9,82–87). After the patient is shifted to move the target to its simulated location relative to the beams, treatment proceeds as planned. Online methods correct for systematic and random error as well as some anatomical changes such as the effects of rectal and bladder filling on abdominal tumors. Limiting factors are the time to perform the comparison and the accuracy with which the correction can be made.

Offline strategies aim to reduce Δ, which often dominates the CTV-PTV margin. Imaging without correction is performed at the first few treatments. The setup error is analyzed and the correction (usually a shift) is made after a number of sessions determined by protocol. No-action-level protocols image for N sessions, correct before the treatment number N + 1, and thereafter image less frequently to detect time trends which are corrected according to a second protocol.88,89 Simulation studies agree that the “optimal” number of imaging sessions is small (∼3–5). Shrinking action level protocols reduce the action level (e.g., by a factor of N−1/2) at each treatment session, cutting off at ∼5 sessions to decide that no correction is needed. The process restarts after each correction and also proceeds to a second-stage protocol to detect and correct for time trends.90,91

Adaptive radiotherapy (ART) takes the offline correction strategy to a higher level.92 The initial treatments (e.g., first five) are based on a PTV with generic margins and imaging is performed at each treatment. Based on the imaging, a new, patient-specific PTV is defined and a new treatment plan is generated and used for the remaining treatments. Current developments in ART, as implemented on conventional linacs and tomotherapy units is described in the Proceedings of the 2006 AAPM Summer School.9

III.E. Looking forward

Despite the widespread use and acceptance of the margin and PTV concept, there are limitations. Geometric errors such as setup error and motion are being accounted for by increasing the size of the PTV. But, it would be preferable to include the uncertainties where they naturally occur: random setup error can be included as fluence convolution,93 random internal motion approximated by dose convolution,94 etc. Incorporating systematic errors involves many dose computations, but this is being investigated by several groups.95,97

The elimination of the geometric margin and PTV concept in favor of probabilistic planning is fraught with challenges and complexity, and the PTV will likely be with us for some time to come. Software tools to more formally account for geometric errors in radiotherapy and obviate the margin and PTV concepts are still being developed. This is ironic because IGRT methods to reduce uncertainty are also being developed. Thus, the necessary margins are smaller and the impact of issues arising from the PTV concept is reduced.

IV. CRANIAL STEREOTACTIC RADIOSURGERY: A SPECIAL CASE OF SETUP ERROR MANAGEMENT

Stereotactic radiosurgery (SRS) is a radiotherapy technique that places high demands on both precision and accuracy. In its original (and still widely used) implementation, SRS treats small (typically ≤4 cm) intracranial lesions in a single high dose fraction and setup error is controlled by stringent physical immobilization using head frames98 or bite plates.99 SRS was pioneered early in the 1950s by Leksell100 and physicist colleagues, using first multiple x-ray beams and later a large number of 60Co sources in the Gamma Knife. SRS with particle beams has also been available for decades, and the second half of the 1980s saw the implementation of linac-based SRS101,102 including complex techniques that involved simultaneous gantry and couch motion.103 This culminated in the development of sophisticated SRS techniques which can be used for both intracranial and extracranial SRS such as micro multileaf collimators available from several vendors and the frameless image-guided robot-mounted CyberKnife (Accuray). Early developments of these systems were reported by Cosgrove et al.104 and Adler et al.105 Differences in dose distributions between
V. RESPIRATORY MOTION: A SPECIAL PROBLEM

V.A. Introduction

Respiratory motion management addresses errors introduced during the imaging and delivery processes from breathing-induced motion. Although the complexity of issues arising from breathing motion deserves separate consideration, interfraction changes and respiratory motion are often dealt with simultaneously and target delineation uncertainty introduces errors of similar or greater magnitude. Motion management is one of the most topical issues in modern radiotherapy, and medical physicists are playing a key role in the development and implementation of this technology.

The strategies to deal with motion can be separated into motion inclusive methods, motion reduction methods (abdominal compression and breath-hold), respiratory gating, and target tracking. There are different combinations of CT imaging and delivery as shown in Fig. 2. Treatment planning aspects for each of these combinations is beyond the scope of this article. For all of these approaches a method of in-room imaging is desired, and there are several options.

V.B. CT imaging

Respiratory motion induces artifacts in 3D CT scans.\textsuperscript{114,115} One method of accounting for this motion is to use a respiratory signal to trigger the CT scanner to acquire data. If the trigger occurs at the same part of the breathing cycle for each image slice, the CT scan is useful for planning respiratory gated or tumor tracking treatment. A second method that is increasingly used is “4D CT” or respiration-correlated CT (R CCT), where multiple images, covering the full breathing cycle, are acquired for each slice. If these are retrospectively sorted, the user can create a CT movie to visualize the breathing motion of the tumor and other anatomy.

Breath-hold methods using “deep inspiration breath-hold”\textsuperscript{116–118} or “active breathing control”\textsuperscript{119,120} allow the acquisition of scans at a single breath-hold state. This method is restricted to patients who can perform several reproducible breath-holds at simulation and then repeat performance as many times as necessary to get through each daily treatment. For lung cancer patients with this capability, deep inspiration can both reduce tumor motion and substantially increase the lung volume, thereby decreasing the fractional volume of normal lung being irradiated.

Abdominal compression involves the application of significant pressure to the abdomen, typically just inferiorly to the sternal notch. Compression has been demonstrated to reduce respiratory motion in most cases\textsuperscript{121} Thus, scanning and treating with compression should result in reduced respiratory-induced motion.

It should be noted that residual motion and resulting artifacts affect imaging with all these approaches, and scans used for treatment planning should be carefully evaluated. Irregular respiration in particular affects gated and 4D CT scans.

Audiovisual biofeedback is a method that may improve the quality of gated and 4D CT scans.\textsuperscript{122–126} Although such techniques are beyond their usual domain of interest, physicists have been bringing them into the radiation therapy setting. Audiovisual biofeedback has been shown to reduce respiratory variability which is known to cause artifacts in 4D CT scans.\textsuperscript{127,128} 4D CT scan acquisition may also be improved by changes to the acquisition method\textsuperscript{129} which have not been developed significantly since the initial implementation of 4D CT. Postprocessing of 4D CT scans can further increase the utility and accuracy of this technology.

V.C. Treatment delivery

Several articles describing the clinical implementation and results of respiratory motion management have been written.\textsuperscript{82–87} It could be argued that motion management has facilitated the increase in interest and application of extracranial stereotactic radiotherapy. However, to date, there are no prospective data comparing the outcomes of treatment with and without motion management. Work by Fang et...
VI. NEW METHODS

VI.A. Cone beam CT (CBCT)

Portal imaging with MV treatment beams has proven to be useful in preventing gross patient setup errors, but MV radiographs suffer from poor tissue contrast and often can only help to align bony anatomy. The need for volumetric tissue information during treatment for accurate target positioning spurred on the development of tomographic imaging techniques. The pioneering work was done in the early 1980s by Swindell,131 working first in North America and later in England. The original devices looked like third-generation CT arc detector arrangements. Much of the initial development took place slightly later, in Europe and North America, with Brahme132 working on MVCT for a 50 MV Racetrack linac and Lewis et al.133 and Cho et al.134 for conventional linacs. The first to propose the use of an electronic portal imager for MVCT appears to be Jaffray et al.135 and Midgley et al.136 in the early 1990s. Later developments came from Mosleh-Shirazi et al.137 for a conventional linac and Ruchala et al.138 for a tomotherapy system. MV imaging systems, however, have a low detection efficiency, and lateral electron transport in the detector tends to degrade the spatial resolution. Therefore, several groups returned to the old idea of mounting a kV x-ray unit on a radiotherapy head to provide images with higher contrast for treatment verification. Biggs et al.139 described a linac-mounted x-ray tube in 1985, but it was not until the mid-nineties that Jaffray and the Beaumont team140 made major efforts to develop a mature technology. Nowadays, newly purchased linacs from most manufacturers come with on-board kV or MV CT treatment verification systems.

A major advantage of CBCT images over conventional CT images, besides the obvious fact that the images are acquired on the treatment couch and very close to treatment time, is that they have superior spatial resolution in coronal and sagittal reconstruction planes, allowing more accurate organ delineation. One major disadvantage is the image degradation by scatter, which is a topic that is currently under scrutiny. Two other disadvantages—the time (~1 min) and imaging dose of a full CBCT scan—may be ameliorated in some cases through digital tomosynthesis. This technique uses the on-board imaging equipment but requires shorter rotation segments (40°–80°) (Ref. 141) than CBCT and acquires images that are superior to plain radiographs for soft tissue localization. Since CBCT images represent the true treatment geometry, explorations into their direct use for more accurate dose calculations have been undertaken (Lagen et al.142). CBCT with either kV or MV x rays is currently a much investigated topic, as seen from the review in the Proceedings of the 2006 AAPM Summer School.143

VI.B. Ultrasound guidance

Ionizing radiation has certain disadvantages for treatment verification imaging including the possibility of relatively high radiation dose to healthy tissue, and the cost of on-board cone beam imagers or CT scanners in treatment rooms. Therefore, since the mid-nineties there have been efforts to integrate the well-known diagnostic technique of ultrasound imaging (US) into treatment rooms for daily target localization. US imaging has an intrinsically high spatial resolution (sub-millimeter), delivers no harmful dose, and is a relatively cheap technology. By far the largest effort went into prostate localization, but applications in imaging of liver, pancreas, breast, and cervix have also received attention.

Because most prostate adenocarcinoma occurs in the peripheral zone of the gland, successful treatment requires adequate irradiation of the periphery. In current practice, treatment margins are nearly always designed using a population-based margin recipe as described above. The margin is then kept fixed throughout the treatment course. But, individualized margins might be preferable in terms of healthy tissue sparing (e.g., rectum in the case of prostate cancer) and dose escalation.

The implementation of 2D and 3D US imaging for daily target localization occurred almost entirely in North America and has been very much physicist-driven. The first 2D US system dedicated to prostate localization, known as the BAT, was introduced about 10 years ago. The system compared the daily US prostate images taken in the treatment room to a reference CT image acquired at simulation. Lattanzi et al.144 were among the first to report on the clinical performance of this system. The BAT is an intermodality system in that it registers an US image to a CT image, which may lead to CT definition uncertainties that translate directly into systematic uncertainties in the BAT alignments. Workers who compared...
the BAT against implanted markers for portal imaging localization\textsuperscript{139} found systematic differences of several millimeters between the two methods. These authors generally assume the marker method represents the gold standard technique, but random marker movements limited to 2 mm have been observed.\textsuperscript{145} The same group reports significant interobserver variation in US prostate alignment.

As a later development, Bouchet \textit{et al.}\textsuperscript{146} introduced 3D ultrasound imaging with infrared spatial localization of the US probe. This led to the development of various commercially available 3D US systems including one that directly compares 3D US images taken at simulation to daily 3D US images taken just before treatment. This may reduce the systematic errors reported in some of the above-mentioned studies.\textsuperscript{147} Orton \textit{et al.}\textsuperscript{148} investigated the impact of daily US shifts on the accuracy of dose distributions in the target and surrounding organs for prostate treatment. They found only small dose differences when organ shifts were performed, but this may depend on the type of dose calculation algorithm.

US target localization is not yet a fully matured technique. Issues such as interobserver variability, difficulties of standardizing scanning techniques, and organ motion due to probe pressure\textsuperscript{149} all affect treatment verification accuracy and call for further investigation. A current AAPM task group is developing guidelines for the QA of these systems.

\section*{VI.C. Advanced image guidance}

\subsection*{VI.C.1. Introduction}

Image-guided radiotherapy (IGRT) is a relatively new term but not a new concept. What is changing is the frequency with which we are obtaining imaging information before and during treatment, the number of patients who receive IGRT, and the challenges of optimally using this information to adjust the treatment plan and guide the treatment delivery.

\subsection*{VI.C.2. IGRT evolution example}

IGRT is in widespread clinical practice. The proceedings of the 2006 AAPM Summer School are an excellent source of information about this burgeoning field. An example of how rapidly IGRT is changing clinical practice is in the comparison of two Radiation Therapy Oncology Group\textsuperscript{150} (RTOG) trials, 0117 (2001) and 0617 (2006), as seen in Table I. Trial 0117 was a phase I/II dose escalation trial of 3D-CRT combined with a specified concurrent chemotherapy for treatment of medically inoperable non-small-cell lung cancer (NSCLC). Trial 0617 was a randomized phase III comparison of chemotherapy concurrent with either the community standard dose of 60 Gy (2 Gy/fraction) or with the maximum tolerated dose of 74 Gy (2 Gy/fraction) determined by trial 0117. The dose calculation algorithm requirements in 0617 are for a superposition/convolution class algorithm. In 0117 no correction was allowed for the prescription. Though not always considered IGRT, clearly dose and geometry are interrelated and thus errors in dose calculation are analogous to geometry errors that IGRT methods are attempting to improve. Furthermore, though there are margin formulas to account for geometric uncertainty, no such formulas exist to account for dose calculation uncertainty. 4D thoracic CT scanning to estimate tumor motion and use for planning was not mentioned in 0117—indeed, it had not been invented when the protocol was developed. The motion management strategy in 0117 was to increase margins if motion was observed. 0617 requires a demonstration of motion reduction to less than 1 cm. PET imaging was not mentioned in 0117, and is strongly encouraged in 0617. Clearly, the changes in the clinical trial design reflect a change in the general clinical practice of radiotherapy and an acceptance of the value of IGRT strategies in radiotherapy. It will be interesting to see this evolution of IGRT to a possible “1117” trial in 2011, “1617” trial in 2016, and beyond.

\section*{VI.D. Looking forward}

The number and modalities of imaging procedures performed before, during, and after treatment are increasing. Imaging for treatment planning allows improved information for target delineation, assessing normal tissue functional status, and tumor physiology, e.g., hypoxic status. Imaging during treatment has many applications. Clearly the images can be used for treatment beam guidance. Online or offline adaptation of the treatment plan, in response to more subtle cues than setup error (e.g., tumor shrinkage or growth) is now possible. Additionally, imaging during treatment allows an assessment of the patient response to the treatment regime which may combine adjuvant targeted agents with radiotherapy. Imaging for treatment response allows either the individual tailoring of the dose and prescription or a radical change in treatment. Post-treatment imaging yields crucial information on dose-response, and can also be an early indicator of toxicity or recurrence which can be managed before clinical symptoms arise.

During treatment the integration of imaging systems with the radiation delivery is allowing more intelligent and automated use of the imaging data for treatment guidance, improving both treatment accuracy and also efficiency.

The RTOG has embraced image guidance, and it is anticipated that other trial groups will require advanced imaging, planning, and delivery for the radiotherapy portion of clinical trials.
The greatest advances in radiotherapy over the past 50 years have been technical in nature. Medical physicists, through research, development, and clinical efforts, and the AAPM through its Task Groups, education initiatives, meetings, and publications have contributed significantly to attaining the current state of the art of radiation treatment accuracy and precision. It is worth taking a moment to think about, and acknowledge, the pioneering efforts in our field. Clearly these contributions will continue with the current generation of medical physicists. As our ability to conform to changing anatomy develops, the emphasis of future development in radiotherapy will move toward including tumor and changing anatomy develops, the emphasis of future development in radiotherapy will move toward including tumor and normal tissue physiology into everyday radiotherapy. The skills and knowledge required for future research and development will evolve with time, but the process of problem identification, solution, implementation, and validation, core to a medical physicist’s training, will remain.

VII. SUMMARY

The Board

Medical Physics, Vol. 35, No. 3, March 2008

836 Yorke, Keall, and Verhaegen: Treatment accuracy and precision

1E. T. Farmer, J. F. Fowler, and J. W. Haggith, “Megavoltage treatment planning and the use of xeroradiography,” Br. J. Radiol. 36, 426–435 (1963).
2K. P. Doppel, in Ref. 7, pp. 447–461.
3J. van Dyk, in The Modern Technology of Radiation Oncology, edited by J. van Dyk (Medical Physics Publishing, Madison, WI, 1999), pp. 95–129.
4H. E. Johns and J. R. Cunningham, The Physics of Radiotherapy (Charles C. Thomas, Springfield, IL, 1983), pp. 426–434.
5G. E. Hanks, J. J. Diamond, and S. Kramer, “The need for complex technology in radiation oncology. Correlations of facility characteristics and structure with outcome,” Cancer 55 (Suppl.), 2198–2201 (1985).
6M. Goitein and M. Abrams, “Multi-dimensional treatment planning. I. Delineation of anatomy,” Int. J. Radiat. Oncol. Biol. Phys. 9, 777–787 (1983).
7M. Goitein, M. Abrams, D. Rowell, H. Pollari, and J. Wiles, “Multi-dimensional treatment planning. II. Beam’s eye-view, back projection, and projection through CT sections,” Int. J. Radiat. Oncol. Biol. Phys. 9, 789–797 (1983).
8M. Goitein and T. Miller, “Planning proton therapy of the eye,” Med. Phys. 10, 275–283 (1983).
9J. Malvin, A. Turrisi, and E. Cheng, in Ref. 7, pp. 462–478.
10M. Goitein, “Limitations of two-dimensional treatment planning programs,” Med. Phys. 9, 580–586 (1982).
11M. Goitein, J. W. Wong, and W. B. Harms, in Ref. 7, pp. 495–511.
12A. L. Boyer, “Patient positioning and immobilization devices,” in Radiation Oncology Physics—1986, edited by J. G. Kereiakes, H. R. Elson, and American Institute of Physics, New York, 1987.
13J. A. Purdy, J. W. Wong, and W. B. Harms, in Ref. 7, pp. 495–511.
14D. L. McShan, A. Silverman, D. M. Lanza, L. E. Weinstein, and A. Glicksman, “A computerized three-dimensional treatment planning system utilizing interactive colour graphics,” Br. J. Radiol. 52, 478–481 (1979).
15G. W. Sherouse, J. D. Bourland, K. Reynolds, H. L. McMurry, T. P. Mitchell, and E. L. Chaney, “Virtual simulation in the clinical setting: Some practical considerations,” Int. J. Radiat. Oncol. Biol. Phys. 15, 1059–1065 (1989).
16G. W. Sherouse, K. Novins, and E. L. Chaney, “Computation of digitally reconstructed radiographs for use in radiotherapy treatment design,” Int. J. Radiat. Oncol. Biol. Phys. 18, 651–658 (1990).
17G. T. Y. Chen, C. A. Pelizzari, D. R. Selibring, and M. Kessler, in Ref. 7, pp. 595–608.
18K. P. Doppel, in Ref. 7, pp. 447–461.
19L. E. Reinstein, “Radiotherapy portal imaging quality,” in Ref. 7, pp. 627–655.
20B. Fraass, in Advances in Radiation Oncology Physics: Dosimetry, Treatment Planning, and Brachytherapy, edited by J. A. Purdy (American Institute of Physics, Woodbury, NY, 1992), pp. 967–997.
21J. A. Purdy, R. L. Gerber, and W. B. Harms, in Ref. 39, pp. 524–534.
22G. W. Sherouse, in Ref. 39, pp. 925–947.
23J. E. Marks, A. G. Haus, H. G. Sutton, and M. L. Griem, “The value of frequent treatment verification films reducing localization error in the irradiation of complex fields,” Cancer 37, 2755–2761 (1976).
24L. E. Reinstein, H. I. Amols, P. J. Biggs, R. T. Droge, W. R. Filimonov, W. R. Lutz, and S. Shalev, “Radiotherapy Portal Imaging Quality: AAPM Report No. 24,” American Institute of Physics, 1987.
25L. E. Reinstein, M. Durham, M. Telft, A. Yu, A. S. Glicksman, and W. Eaton, “Portal film quality: A multiple institutional study,” Med. Phys. 11, 555–557 (1984).
26G. J. Kutcher, G. S. Mageras, and S. A. Liebel, “Control, correction, and modeling of setup errors and organ motion,” Semin. Radiat. Oncol. 5, 134–145 (1995).
27L. E. Reinstein, H. I. Amols, P. J. Biggs, A. B. Droge, A. B. Filimonov,
W. Lutz, and S. Shalev. Radiation Therapy Portal Imaging Quality: AAPM Report No 24, Report of AAPM Task Group No. 28, American Institute of Physics, 1987.

6. S. Shalev, “Megavoltage Portal Imaging,” in Teletherapy: Present and Future, Proceedings of the 1996 Summer School, edited by T. R. Mackie and J. R. Palta (Advanced Medical Publishing, Madison, WI, 1996), pp. 445–469.

7. J. M. Balter, R. K. Ten Haken, and K. L. Lam, “Treatment Setup Verification,” presented at Teletherapy: Present and Future. Proceedings of the 1996 Summer School, Madison, WI, 1996.

8. N. A. Baily, R. A. Horn, and T. D. Kamp, “Fluorescopic visualization of megavoltage therapeutic x ray beams,” Int. J. Radiat. Oncol. Biol. Phys. 6, 935–939 (1980).

9. A. L. Boyer, L. Antonuk, A. Fenster, M. Van Herk, H. Meertens, P. Munro, L. E. Reinstein, and J. Wong, “A review of electronic portal imaging devices (EPIDs),” Med. Phys. 19, 1–16 (1992).

10. ICRU Report 50, “Prescribing, recording and reporting proton beam therapy,” International Commission on Radiation Units and Measurements, Bethesda, MD, 1997.

11. M. G. Herman, J. M. Balter, D. A. Jaffray, K. P. McGee, P. Munro, S. Shalev, M. Van Herk, and J. W. Wong, “Clinical use of electronic portal imaging: Report of AAPM Radiation Therapy Committee Task Group 58,” Med. Phys. 28, 712–737 (2001).

12. P. Munro, “Portal imaging technology: Past, present, and future,” Semin. Radiat. Oncol. 5, 115–133 (1995).

13. S. K. Khoo and D. L. Joon, “New developments in MRI for target volume delineation in radiotherapy,” Br. J. Radiol. 79, Spec. No. 1, S2–S15 (2006).

14. C. C. Ling, J. Humm, S. Larson, H. Amols, Z. Fuks, S. Leibel, and J. A. Koutcher, “Towards multidimensional radiotherapy (MD-CRT): Biological imaging and biological conformity,” Int. J. Radiat. Oncol. Biol. Phys. 47, 551–560 (2000).

15. J. A. Pelizzari, in Intensity-Modulated Radiation Therapy: The State of the Art, AAPM Medical Physics Monograph #29, edited by J. R. Palta and T. R. Mackie (Medical Physics Publishing, Madison, WI, 2003), pp. 139–192.

16. J. I. Rosenman, E. P. Miller, G. Tracton, and T. J. Cullip, “Image registration: An essential part of radiation therapy treatment planning,” Int. J. Radiat. Oncol. Biol. Phys. 40, 197–205 (1998).

17. P. Giraud, G. Kantor, H. Loiseau, and K. E. Rosenzweig, “Target definition in the thorax and central nervous system,” Semin. Radiat. Oncol. 15, 146–155 (2005).

18. T. Bortfeld, M. van Herk, and S. B. Jiang, “When should systematic target margin be used?” Semin. Radiat. Oncol. 15, 136–145 (2005).

19. V. Gregoire, A. Bol, X. Geets, and J. Lee, “Is PET-based planning the new standard in modern radiotherapy? The head and neck paradigm,” Semin. Radiat. Oncol. 16, 232–238 (2006).

20. G. J. Kutcher et al., “Comprehensive QA for radiation oncology: Report of AAPM Radiation Therapy Committee Task Group 40,” Med. Phys. 21, 581–618 (1994).

21. M. G. Herman, T. M. Pisansky, J. J. Kruse, J. I. Prisciandaro, B. J. Davis, and B. F. King, “Technical aspects of daily online positioning of the prostate for three-dimensional conformal radiotherapy using an electronic portal imaging device,” Int. J. Radiat. Oncol. Biol. Phys. 57, 1131–1140 (2003).

22. G. J. Kutcher et al., “Comprehensive QA for radiation oncology: Report of AAPM Radiation Therapy Committee Task Group 40,” Med. Phys. 21, 581–618 (1994).

23. S. L. Meeks, W. A. Tome, L. G. Bouchet, A. C. Hass, J. M. Buatti, and F. J. Bova, in Intensity-Modulated Radiation Therapy: The State of the Art, edited by J. R. Palta and T. R. Mackie (Medical Physics Publishing, Madison, WI, 2005).

24. O. T. Le, B. W. Loo, A. Ho, C. Cotruzz, A. C. Koong, H. Wakelee, S. T. Kee, D. Constantinescu, R. I. Whyte, and J. Donington, “Results of a phase I dose-escalation study using single-fraction stereotactic radiotherapy for lung tumors,” J. Thorac. Oncol. 1, 802–809 (2006).

25. D. L. Lutzenberg, L. A. Dawson, H. Sandler, M. G. Sanda, D. L. McShan, R. K. Ten Haken, K. L. Lam, K. K. Brock, and J. M. Balter, “Daly prostate targeting using implanted radiopaque markers,” Int. J. Radiat. Oncol. Biol. Phys. 52, 699–703 (2002).

26. H. Onishi, K. Kuriyama, T. Komiyama, S. Tanaka, N. Sano, Y. Aikawa, Y. Tateda, T. Araki, S. Ikenga, and M. Uematsu, “A new irradiation system for lung cancer combining linear accelerator, computed tomography, patient self-breathing control, and patient-directed beam control without respiratory monitoring devices,” Int. J. Radiat. Oncol. Biol. Phys. 61, 1010–1015 (2005).

27. H. Onishi et al., “Hypofractionated stereotactic radiotherapy (HypoFX-SRT) for stage I non-small cell lung cancer: Updated results of 257 patients in a Japanese multi-institutional study,” J. Thorac. Oncol. 2, Suppl. 3, S94–S100 (2007).

28. H. Shirato, S. Shimizu, T. Shimizu, T. Nishioka, and K. Miyasaka, “Real-time tumour-tracking radiotherapy,” Lancet 353, 1331–1332 (1999).

29. R. Wagman, E. Yorke, P. Giraud, E. Ford, K. Sidhu, G. Mageras, B. Minsky, and K. Rosenzweig, “Reproducibility of organ position with respiratory gating for liver tumors: Use in dose-escalation,” Int. J. Radiat. Oncol. Biol. Phys. 55, 659–668 (2003).

30. T. Bortfeld, M. Van Herk, and S. B. Jiang, “When should systematic patient positioning errors in radiotherapy be corrected?” Phys. Med. Biol. 47, N297–N302 (2002).
112M. Heydarian, P. W. Hoban, and A. H. Beddoe, “A comparison of dosimetry with clinical practice in stereotactic radiosurgery for brain tumors,” Med. Phys. 34, 202–214 (2007).

113F. Colombo, A. Benedetti, F. Pozza, R. C. Avanzo, C. Marchetti, G. Chirurgo, and A. Zanardo, “External stereotactic irradiation by linear accelerator,” Neurosurgery 40, 405–407 (2000).

114E. B. Podgorsak, A. Olivier, M. Pla, P. Y. Lefebvre, and J. Hazelt, “Dose-response dual-isocenter stereotactic radiosurgery,” Acta Radiol. 38, 875–882 (1997).

115L. Leksell, “The stereotactic method and radiosurgery of the brain,” Acta Radiol. 38, 102, 316–319 (1951).

116J. R. Adler, Jr., M. J. Murphy, S. D. Chang, and S. L. Hancock, “Image-guided robotic radiosurgery,” Neurosurgery 42, 1299–1306 (1999); see also the Discussion on pp. 1306–1307.

117C. Yu, G. Jozsef, M. L. Apuzzo, and Z. Petrovics, “Dosimetric comparison of CyberKnife with other radiosurgical modalities for an endovascular target,” Neurosurgery 55, 1155–1162; see also the Discussion on pp. 1162–1163 (2000).

118M. C. Schell, F. J. Bova, D. A. Larson, D. D. Keavitt, W. R. Lutz, E. B. Podgorsak, and A. Wu, Stereotactic Radiosurgery (American Association of Physicists in Medicine, Madison, WI, 1995).

119M. J. Murphy, “The importance of computed tomography slice thickness in radiographic patient positioning for radiosurgery,” Med. Phys. 26, 171–175 (1999).

120T. D. Solberg, J. J. DeMarco, F. E. Holly, J. B. Smathers, and A. A. DeSalles, “Monte Carlo treatment planning for stereotactic radiosurgery,” Radiat. Oncol. 49, 73–84 (1998).

121T. D. Solberg, F. E. Holly, A. A. De Salles, R. E. Wallace, and J. B. Smathers, “Implications of tissue heterogeneity for radiosurgery in head and neck tumors,” Int. J. Radiat. Oncol. Biol. Phys. 32, 235–239 (1995).

122R. K. Rice, J. R. Hansen, G. K. Svensson, and R. L. Siddon, “Measurements of dose distributions in small beams of 6 MV x-rays,” Phys. Med. Biol. 32, 1087–1099 (1987).

123M. Heydarian, P. W. Hoban, and A. H. Beddoe, “A comparison of dosimetry techniques in stereotactic radiosurgery,” Med. Phys. Biol. 41, 93–110 (1996).

124F. Verhaegen, J. J. Das, and H. Palmas, “Monte Carlo dosimetry study of a 6 MV stereotactic radiosurgery unit,” Phys. Med. Biol. 43, 2755–2768 (1998).

125J. M. Balter, R. K. Ten Haken, T. S. Lawrence, K. L. Lam, and J. M. Robertson, “Uncertainties in CT-based radiation therapy treatment planning associated with patient breathing,” Int. J. Radiat. Oncol. Biol. Phys. 26, 167–174 (1996).

126J. P. Keall, G. S. Mageras, J. M. Balter, R. S. Emery, K. M. Forster, S. B. Jiang, F. M. Kapatoes, D. A. Low, M. J. Murphy, B. R. Murray, C. F. Ramsey, M. V. Herk, S. S. Vedam, J. W. Wong, and E. Yorke, “The management of respiratory motion in radiation oncology report of AAPM Task Group 76,” Med. Phys. 33, 3874–3900 (2006).

127J. Hanley, M. D. Debois, D. Mah, G. S. Mageras, A. Raben, K. Rosenzweig, B. Mychalczak, L. H. Schwartz, P. J. Glogewer, W. Lutz, C. C. Ling, S. A. Leibel, Z. Fukus, and G. J. Kutch, “Deep inspiration breath-hold technique for lung tumors: The potential value of target immobilization and reduced lung density in dose escalation,” Int. J. Radiat. Oncol. Biol. Phys. 45, 603–611 (1999).

128D. Mah, J. Hanley, K. E. Rosenzweig, E. Yorke, L. Braban, C. C. Ling, S. A. Leibel, and G. Mageras, “Technical aspects of the deep inspiration breath-hold technique in the treatment of thoracic cancer,” Int. J. Radiat. Oncol. Biol. Phys. 48, 1175–1180 (2000).

129K. E. Rosenzweig, J. Hanley, D. Mah, G. Mageras, M. Hunt, S. Toner, C. Burner, C. C. Ling, B. Mychalczak, Z. Fukus, and S. A. Leibel, “The deep inspiration breath-hold technique in the treatment of inoperable non-small-cell lung cancer,” Int. J. Radiat. Oncol. Biol. Phys. 48, 81–87 (2000).

130M. Remouchamps, N. Lees, F. A. Vicini, M. B. Sharpe, L. L. Kestin, P. Y. Chen, A. A. Martinez, and J. W. Wong, “Initial clinical experience with moderate deep-inspiration breath hold using an active breathing control device in the treatment of patients with left-sided breast cancer using external beam radiation therapy,” Int. J. Radiat. Oncol. Biol. Phys. 56, 704–715 (2003).

131J. W. Wong, M. B. Sharpe, D. A. Jaffray, V. R. Kini, J. M. Robertson, J. S. Stromberg, and A. A. Martinez, “The use of active breathing control (ABC) to reduce margin for breathing motion,” Int. J. Radiat. Oncol. Biol. Phys. 44, 911–919 (1999).

132Y. Negoro, Y. Nagata, T. Aoki, T. Mizowaki, N. Araki, K. Takayama, M. Kokubo, S. Yano, S. Koga, K. Sasai, Y. Shibamoto, and M. Hiraoka, “The effectiveness of an immobilization device in conformal radiotherapy for lung tumor: Reduction of respiratory tumor movement and evaluation of the daily setup accuracy,” Int. J. Radiat. Oncol. Biol. Phys. 50, 889–898 (2001).

133R. George, T. D. Chung, S. S. Vedam, V. Ramakrishnan, R. Mohan, E. Wotjak, and P. J. Keall, “Audio-visual biofeedback for respiratory-gated radiotherapy: Impact of audio instruction and audio-visual biofeedback on respiratory-gated radiotherapy,” Int. J. Radiat. Oncol. Biol. Phys. 65, 924–933 (2006).

134R. George, V. Ramakrishnan, J. V. Siebers, T. D. Chung, and P. J. Keall, “Investigation of patient, tumour and treatment variables affecting residual motion for respiratory-gated radiotherapy,” Phys. Med. Biol. 51, 5303–5319 (2006).

135R. George, S. S. Vedam, T. D. Chung, V. Ramakrishnan, and P. J. Keall, “Respiratory-motion compensation in the sinusoidal model to lung cancer patient respiratory motion,” Med. Phys. 32, 2850–2861 (2005).

136T. Neicu, R. Berbeco, J. Wolfgang, and S. B. Jiang, “Synchronized moving aperture radiation therapy (SMART): Improvement of breathing pattern reproducibility using respiratory coaching,” Phys. Med. Biol. 51, 617–636 (2006).

137M. Stock, K. Kontirova, K. Dieckmann, J. Bogner, R. Poetter, and D. Mah, “Development and application of a real-time monitoring and feedback system for deep inspiration breath hold based on external marker tracking,” Med. Phys. 33, 2868–2877 (2006).

138A. F. Abdelnour, S. A. Nehme, T. Pan, J. L. Humm, P. Vernon, H. Schoder, K. Rosenzweig, G. Mageras, E. Yorke, S. M. Larson, and Y. Erdi, “Phase and amplitude binning for 4D-CT imaging,” Phys. Med. Biol. 52, 3515–3529 (2007).

139Y. D. Mutfal, J. A. Antolak, and D. H. Brinkmann, “The impact of temporal inaccuracies on 4DCT image quality,” Med. Phys. 34, 1615–1622 (2007).

140P. J. Keall, S. S. Vedam, R. George, and J. F. Williamson, “Respiratory regularity gated 4D CT acquisition: Concepts and proof principle,” Australas. Phys. Eng. Sci. Med. 30, 211–220 (2007).
L. C. Fang, R. Komaki, P. Allen, T. Guerrero, R. Mohan, and J. D. Cox, “Comparison of outcomes for patients with medically inoperable Stage I non-small-cell lung cancer treated with two-dimensional vs. three-dimensional radiotherapy,” Int. J. Radiat. Oncol. Biol. Phys. 66, 108–116 (2006).

W. Swindell, “A 4-MV CT scanner for radiation therapy; spectral properties of the therapy beam,” Med. Phys. 10, 347–351 (1983).

A. Brahme, B. Lind, and P. Nafstadius, “Radiotherapeutic computed tomography with scanned photon beams,” Int. J. Radiat. Oncol. Biol. Phys. 13, 95–101 (1987).

D. G. Lewis, W. Swindell, E. J. Morton, P. M. Evans, and Z. R. Xiao, “A megavoltage CT scanner for treatment verification,” Phys. Med. Biol. 37, 1985–1999 (1992).

J. J. Sonke, R. H. Johnson, and T. W. Griffin, “Cone-beam CT for radiotherapy applications,” Phys. Med. Biol. 40, 1863–1883 (1995).

D. A. Jaffray, “Conebeam CT using fluoroscopic portal imager,” presented at the 4th International Workshop on Electronic Portal Imaging, Amsterdam, 1996.

S. M. Midgley, J. F. Dudson, and R. M. Millar, “A feasibility study for the use of megavoltage photons and a commercial electronic portal imaging area detector for beam geometry CT scanning to obtain 3D tomography data sets of radiotherapy patients in the treatment position,” presented at the 4th International Workshop on Electronic Portal Imaging, Amsterdam, 1996.

A. A. Martinez, and J. W. Wong, “A radiographic and tomographic imaging system integrated into a medical linear accelerator for localization of bone and soft-tissue targets,” Int. J. Radiat. Oncol. Biol. Phys. 45, 773–789 (1999).

F. F. Yin, Z. Wang, S. Yoo, D. Godfrey, and Q. R. Wu, in Integrating New Technologies into the Clinic: Monte Carlo and Image-Guided Radiation Therapy, edited by B. H. Curran, J. M. Balter, and I. J. Chetty (Medical Physics Publishing, Madison, WI, 2006), pp. 471–500.

K. M. Langen, S. L. Meeks, D. O. Poole, T. H. Wagner, T. R. Willoughby, P. A. Kupelian, K. J. Ruchala, J. Haimerl, and G. H. Olivera, “The use of megavoltage CT (MVCT) images for dose recomputations,” Phys. Med. Biol. 50, 4259–4276 (2005).

J. J. Sonke, P. Remeijer, and M. van Herk, in “Room cone beam computed tomography,” in Ref. 141, pp. 543–564.

J. Lattanzi, S. McNeely, W. Pinover, E. Horwitz, I. Das, T. E. Schulteiss, and G. E. Hanks, “A comparison of daily CT localization to a daily ultrasound-based system in prostate cancer,” Int. J. Radiat. Oncol. Biol. Phys. 43, 719–725 (1999).

K. M. Langen, J. Pouliot, C. Anezinos, M. Aubin, A. R. Gottschalk, I. C. Hsu, D. Lowther, Y. M. Liu, K. Shinhara, L. J. Verhey, V. Weinberg, and M. Roach 3rd, “Evaluation of ultrasound-based prostate localization for image-guided radiotherapy,” Int. J. Radiat. Oncol. Biol. Phys. 57, 635–644 (2003).

L. G. Bouchet, S. L. Meeks, G. Goodchild, F. J. Bova, J. M. Buatti, and W. A. Friedman, “Calibration of three-dimensional ultrasound images for image-guided radiation therapy,” Phys. Med. Biol. 46, 559–577 (2001).

F. L. Cury, G. Shenouda, L. Souhami, M. Duclos, S. L. Faria, M. David, F. Verhaegen, R. Corms, and T. Falco, “Ultrasound-based image guided radiotherapy for prostate cancer: Comparison of cross-modality and intra-modality methods for daily localization during external beam radiotherapy,” Int. J. Radiat. Oncol. Biol. Phys. 66, 1562–1567 (2006).

N. P. Orton and W. A. Tome, “The impact of daily shifts on prostate IMRT dose distributions,” Med. Phys. 31, 2845–2848 (2004).

B. Dobler, S. Mai, C. Ross, D. Wolff, H. Wertz, F. Lohr, and F. Wenz, “Evaluation of possible prostate displacement induced by pressure applied during transabdominal ultrasound image acquisition,” Strahlenther. Onkol. 182, 240–246 (2006).

See http://www.rtog.org/