Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 1, Supplement, pp. S33–S37, 2008

0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2007.06.087

QA FOR RT SUPPLEMENT

QUALITY ASSURANCE OF SERIAL 3D IMAGE REGISTRATION, FUSION, AND SEGMENTATION

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Radiotherapy relies on images to plan, guide, and assess treatment. Image registration, fusion, and segmentation are integral to these processes; specifically for aiding anatomic delineation, assessing organ motion, and aligning targets with treatment beams in image-guided radiation therapy (IGRT). Future developments in image registration will also improve estimations of the actual dose delivered and quantitative assessment in patient follow-up exams. This article summarizes common and emerging technologies and reviews the role of image registration, fusion, and segmentation in radiotherapy processes. The current quality assurance practices are summarized, and implications for clinical procedures are discussed. © 2008 Elsevier Inc.

Radiation therapy, Image fusion, Registration, Segmentation, Quality assurance.

INTRODUCTION

Medical images are used routinely to localize targets and normal anatomy in treatment planning and are integral to guiding radiotherapy delivery and assessing response. Image registration establishes the correspondence between modalities and examinations acquired at different points in time and supports targeting in image-guided radiation therapy (IGRT) (1–3). Emerging developments will also improve outcomes analysis by more accurately estimating the actual dose delivered for assessment in patient follow-up examinations.

There is a growing role for image registration and segmentation of anatomic structures in modern radiotherapy. A range of technologies are available to fulfill these requirements. This report provides a brief review of the role of registration and related technologies in radiotherapy processes. Common and emerging technologies are summarized, current quality assurance (QA) practices pertaining to image registration are reviewed, and implications in clinical process design are discussed.

IMAGE REGISTRATION

The spatial relationship between images is established by a transformation model that is optimized through a registration metric. For example, rigid body transforms employ linear translations and rotations. Registration metrics describe the degree of similarity between images, as discussed in the next section. With appropriate tools, rigid registrations are manipulated manually (to achieve a visual match) or automatically using a registration metric.

Figure 1 summarizes general types of transformation models. Rigid transforms currently predominate but are challenged when images acquired at different points in time or location encode nonlinear deformation associated with treatment response, weight change, and variation of organ position and volume between examinations (4–8). Deformable registration can address these challenges, for example, through affine transformations and polynomial (*e.g.,* spline) basis functions, physical viscous-elastic models, and even biomechanical approaches based on the physical malleability of tissue (1, 3, 9–12).

ANATOMIC SURROGATES: REGISTRATION METRICS

Registration metrics describe the degree of numerical similarity between images and are used to optimize transformation models. Registration metrics are derived from anatomic surrogates such as points, line segments, surfaces of the tumor or adjacent organ, or gray-scale intensities. Appropriate

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Conflict of interest: none.

Acknowledgments—We thank the National Cancer Institute of Canada, Terry Fox Foundation; Philips Medical Systems; Varian; and Elekta for sponsoring research related to this article. The authors thank the faculty, students, and staff of Princess Margaret Hospital, especially Laura Dawson, Douglas Moseley, Tim Craig, Olesya Peshko, and David Jaffray.

Received Feb 14, 2007, and in revised form June 19, 2007. Accepted for publication June 20, 2007.

CLASS		ALGORITHM	ATTRIBUTES
Geometric	rigid body		Translation and rotation
	Non-Rigid Body	affine	Translation/rotation with uniform scaling and sheer
		B-spline	Parametric grid with local influence
		thin-plate spline	Weighted anatomic control points with global influence
Physical		Viscous flow/elastic	Explicit voxel displacement by parametric grid in a deforming medium, constrained by intensity gradients
		finite element methods (FEM)	Explicit voxel displacements governed by biomechanical tissue properties, constrained by tetrahedral tissue elements

Fig. 1. Image registration improves the integration of the radiotherapy process.

surrogates account for the clinical objectives in feature alignment in two-dimensional (2D) and three-dimensional (3D) images and reflect the capabilities of the underlying transformation model (13–18). Points and surfaces can be delineated manually, or they can be delineated automatically using intensity gradients or more advanced image processing for surface detection (19).

Manual points or organ surfaces are used widely and successfully but are time-consuming to identify and may ultimately limit registration accuracy in some situations. Gray-scale intensities are an attractive basis for registration metrics because they encompass more information and reduce manual intervention. Gray-scale similarity is calculated by several common methods, with mutual information emerging as a leading approach (1, 3). Automated intensity-based metrics examine the entire image unless efforts are made to direct the focus to areas of clinical importance. If substantial deformation occurs between two images (*e.g.,* neck flexure), then global alignment may by unacceptable. Clip boxes or organ surfaces can be used to direct automated algorithms to focus only on regions deemed important (1).

IMAGE FUSION AND SEGMENTATION

A poorly visualized target on CT may be more grossly visible on MR or PET studies. Registration maps these secondary images and associated target segmentations to the reference planning CT. Combined, or ''fused,'' image intensities allow simultaneous visualization of each imaging modality using a variety of display techniques (1, 3) Such techniques also support the visualization of three-dimensional (3D) dose distributions mapped across imaging modalities.

The previous section mentioned registration metrics formulated from organ surfaces. Organs and target contours have other important roles in planning, guidance, evaluation of dose distributions, and outcomes assessment. Until recently, organ delineation involved manual outlining on transverse images. In some limited cases, tools that follow intensity gradients allowed semiautomated segmentation, but manual ''contouring'' persists as a tedious and time-consuming task. Recently, 3D organ models have emerged as a feasible approach to automated segmentation and a means of reducing contouring effort (19, 20).

REGISTRATION, FUSION, AND SEGMENTATION IN RADIOTHERAPY

Formally, registration aligns images to achieve geometric correspondence, whereas fusion visually maps the complementary data in each modality (1). Clinically, these two functions are closely linked, and referred to almost interchangeably.

Treatment planning

Modern systems support CT-guided planning augmented by additional modalities such as MR and PET. Ideal supplemental examinations are concordant with the planning CT, in both geometry and time. In practice, these modalities are employed at different time points and geographic locations. Because variation in body position, organ filling, and other changes introduce geometric uncertainties, registration by rigid body models should be evaluated carefully to achieve acceptable consistency between modalities. The planning CT is considered the primary model of the patient state over the course of therapy. Differences seen in the secondary modalities are minimized during registration to build a self-consistent static model. ''Four-dimensional CT'' (4DCT) is a unique form of serial imaging that is used to assess organ movement due to breathing over short time interval (21).

4DCT images reconstruct various breathing phases and tend to be registered inherently when acquired in the same scanning session as the primary CT exam. This is also the case for other forms of temporal imaging, which are emerging with the recognition of the importance of vascular architecture and angiogenesis to tumor growth (22).

Treatment delivery

For each fraction of IGRT delivery, the patient is aligned nominally to the machine isocenter. To position the target, images are acquired and registered to the planning CT, and the setup is adjusted to fall within a defined tolerance interval. This process has mainly involved matching megavoltage (MV) portal radiographs with a digitally reconstructed radiograph (DRR) generated from the planning CT. Corrections are implemented by simple couch translations, or manipulation of the patient's position on the couch (14).

Guidance differs from the planning context because images are not perfectly concordant over time. Instead of a static geometry, the images from each treatment session represent a temporal instance of the patient geometry, incorporating residual setup variation, small shifts in the relative position of organs and targets, and other anatomic deformations. Residual setup errors and deformation are undesirable, but they are anticipated and managed using planned target volumes (PTV) margins, for example. The availability of soft-tissue imaging for IGRT has spawned an area of active research and development to understand and mitigate the clinical consequences of residual uncertainties.

Adaptive treatment planning and outcomes assessment

Current applications of IGRT increase targeting accuracy and minimize setup uncertainties through online evaluation using rigid registration. Soft-tissue images also provide record of residual variations and anatomical changes over the treatment course. Experience gained with MV portal imaging has led to strategies that include offline components for determining statistical trends in systematic and random errors (23, 24). Statistics generated with offline strategies support the assessment and adjustment of PTV margins to exploit the precision inherent to an individual's treatment course (25, 26).

Routine IGRT leads naturally to the need to formally ''serialize'' information (*i.e.,* to arrange images in chronological order with registration to the planning context). The transformation model then supports computation and mapping of dose distributions representing individual treatments in the planning reference image, as illustrated in Fig. 2. Deformable registration and anatomic structure mapping provide a better estimate of anatomic changes (Δ) during and subsequent to therapy, as well as accumulation of the actual dose delivered (Σ) (27, 28). Formal dose accumulation may improve the prediction of response, compared with nominal planned distributions. When this process is managed actively during a course of therapy, adaptation to accumulating anatomic changes is possible.

Quality assurance

Image registration in planning and delivery requires verification of the results. Currently, commercial software offers rigid registration. Several groups recommend guidelines for QA of registration in radiosurgery and general planning, many of which are appropriate for IGRT (29–34). The International Atomic Energy Agency (IAEA), for example, emphasizes to the appropriate use of software for the anatomic site and the number of imaging modalities employed. They recommend assessment of the technical principles in use, any bias to a particular modality, constraints imposed on image acquisition, support for 2D or 3D registration (or both), the degree and behavior of automation, the type of model (*i.e.,* rigid or deformable), and dependence on image acquisition parameters or reliance on segmented structures.

The IAEA and American Association of Physicists in Medicine (AAPM) also recommend combined objective and visual queues for evaluating registrations. Recently, the AAPM formed Task Group 132 to review techniques for image registration, to identify issues related to their clinical implementation, to determine the best methods to assess accuracy, and to outline issues related to acceptance and QA.

There is a demand for objective metrics of registration quality within radiotherapy and image-guided surgery (35, 36). Phantom testing can determine whether algorithms reproduce known displacements or changes in orientation under varying conditions (30, 32, 33). Phantoms also help to confirm basic performance metrics, such as geometric scale calibration and orientation, as well as the limits of linearity, accuracy, and precision. However, phantom studies do not completely capture factors degrading registration algorithm performance, such as variations in slice thickness, resolution, distortion, noise, and patient movement. In practice, process QA is required to monitor and manage these factors and to achieve consistent practice.

Setup variation and deformation in individual patients are the most limiting factors in image registration. Fortunately, the cross-comparison of many common imaging modalities inherently includes redundant structures, which help in the visual validation of each patient-specific procedure. This type of qualitative assessment of accuracy can be achieved through image overlay, side-by-side comparison, split-screens, checkerboard displays, and a variety of other visualization techniques (1, 3).

Traditionally, QA of registration tools occurs within the planning context and depends on a limited number of ''upstream'' imaging devices (29, 34) Image registration for planning has been limited to a single event, involving only few staff and a limited need for physicians to delegate decision making. At the same time, delivery guided by radiographs has relied on separate guidelines for QA and clinical practice (37). Imaging data now accompanies planning data when it is transferred to treatment management systems and individual linear accelerators, where it serves as a reference image. Each delivery system, in turn, is capable of generating new data sets that are fed back into planning systems to support vector-based dose accumulation and assessment of anatomical

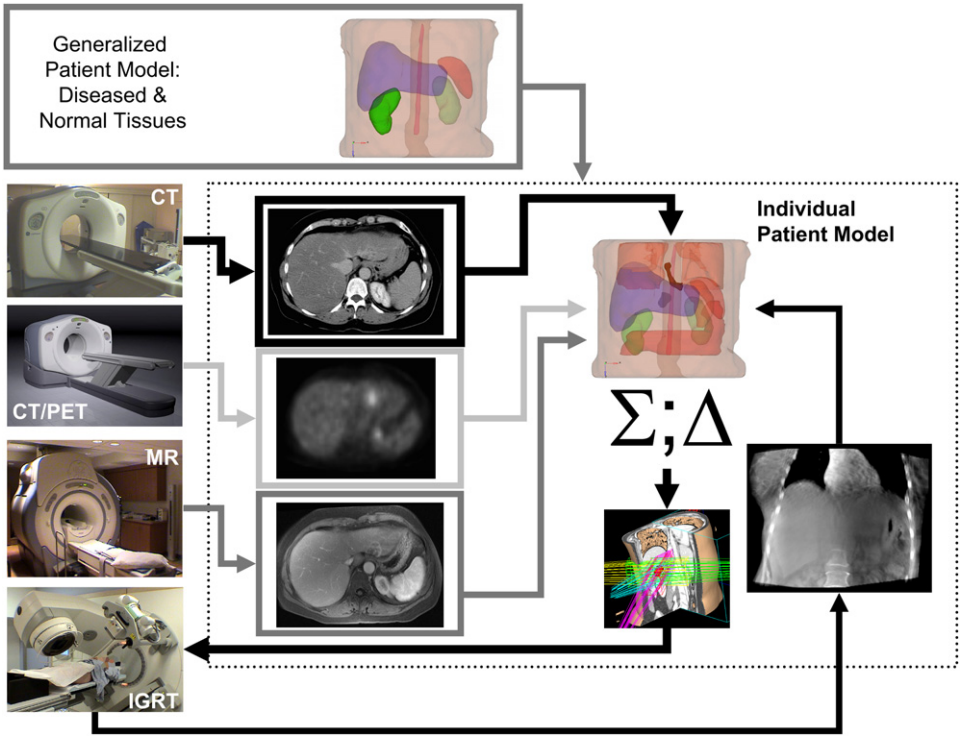

Fig. 2. Image registration in the delivery of image-guided radiotherapy.

changes, as illustrated in Fig. 2. It is likely that images will be stored on externally administered data storage. To complete and evaluate routine volumetric image registration tasks, a stable infrastructure must be maintained. QA programs for equipment and software in the IGRT era must ensure operability and stability spanning across multiple imaging platforms. QA practices must reflect the integration of planning and delivery across information management systems and network infrastructure. Software, knowledge, and decision making are disseminated throughout—and potentially beyond—the radiation therapy department. Consequently, a strong emphasis on standard guidelines for consistent practice and communication of expected results are required to support a working culture that is vigilant to exceptions, and to reduce the burden of patient-specific QA.

CONCLUSIONS

The routine use of IGRT leads to the requirement to ''serialize'' and register each image set to the treatment planning context. The potential to assess anatomic change quantitatively and to perform accurate dose accumulation are some of the anticipated benefits of an integrated approach to IGRT. Radiation therapy supports a strong culture of QA using prescriptive tests for equipment, logical intervals and tolerances for acceptance, commissioning, periodic testing (38). With regard to the specific aspects of image registration, these principles are maintained in recent literature. However, there is no uniform consensus to guide the development of a comprehensive and prescriptive QA program in this arena.

It is feasible to confirm the performance of imaging devices, registration software, and networked storage and retrieval using phantom studies, but there is a strong need to rely on visual checks to ensure consistent and unified practice in individual patient cases. The provision of a robustly tested infrastructure and well-exercised and documented clinical processes will increase confidence in patient-specific situations. To minimize the possibility of human or algorithm error, clinical image acquisition and registration processes should be managed in an integrated fashion where possible, to ensure it is logical, sequential, and reproducible.

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