Journal of Medical Imaging

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Abstract. Image guidance with cone beam computed tomography in radiotherapy can guarantee the precision and accuracy of patient positioning prior to treatment delivery. During the image guidance process, operators need to take great effort to evaluate the image guidance quality before correcting a patient's position. This work proposes an image registration assessment method based on control chart monitoring to reduce the effort taken by the operator. According to the control chart plotted by daily registration scores of each patient, the proposed method can quickly detect both alignment errors and image quality inconsistency. Therefore, the proposed method can provide a clear guideline for the operators to identify unacceptable image quality and unacceptable image registration with minimal effort. Experimental results demonstrate that by using control charts from a clinical database of 10 patients undergoing prostate radiotherapy, the proposed method can quickly identify out-of-control signals and find special cause of out-of-control registration events. © 2018 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.5.2.021221](https://doi.org/10.1117/1.JMI.5.2.021221)]

Keywords: radiotherapy image guidance; control chart monitoring; image registration assessment.

Paper 17254SSR received Aug. 28, 2017; accepted for publication Feb. 1, 2018; published online Mar. 14, 2018.

1 Introduction

Contemporary radiotherapy can be delivered with daily image guidance correction to improve the accuracy and precision of radiation delivery.^{1,2} Image-guided radiation therapy (IGRT) through CBCT has been reported to provide an accurate method for correcting patient position in daily image guidance.^{3–5} Precise delivery of radiotherapy will require staff at the treatment unit to make more decisions on the image guidance quality: is the daily image suitable for registration? Is the image registration acceptable? Is the patient positioned within tolerance? Is the patient position deformed with respect to the planning CT? To achieve these, operators often need to make a great effort on the assessment of image registration quality before correcting a patient's position. Therefore, speeding up the evaluation of image registration quality is helpful for widespread clinical implementation for IGRT.⁶ This work focuses on studying an effective image registration assessment approach to identify unacceptable image quality and unacceptable image registration for IGRT under minimal effort.

The statistical process control (SPC) is the conversion of data to information using statistical techniques to correct and improve process performance. Since SPC was first used in quality control,⁷ it has been widely applied for controlling and monitoring of the production process.^{8–10} Because SPC can provide a quick and calculatingly simple means to evaluate the quality of image registration without the need for operator review, the tools of SPC were applied to the treatment planning and delivery process to ensure a consistently high level of performance in recent years.^{11–15} For example, Pawlicki et al.¹² reported the use of SPC for monitoring linear accelerator beam calibration, Breen et al.¹³ proposed using SPC concepts to analyze the

measurements from head and neck treatment plans, Ung and Wee¹⁴ examined SPC for ensuring good fiducial matching in IGRT, and Able et al.¹⁵ used SPC to study in-phantom high-dose rate treatments.

Image registration is used to determine relative displacements of a pair of images by minimizing a cost function.^{16–19} For each particular patient in the absence of special cause variation, the minimized cost function can be described by a mean and measure of dispersion. Studied reports have shown that image registration based on prostate-implanted fiducial markers can significantly improve localization of the target organ.¹⁴ Fiducial-based image registration algorithms usually use a point-based rigid-body transformation to minimize the distance between corresponding fiducial points in a given portal image.⁵ IGRT with fiducial markers (FMs) may provide an accurate method for internal prostate motion correction, yet there has been an increasing concern regarding safety and efficiency due to transrectal implantation of FMs.²⁰ Therefore, an alternative IGRT method is to use CBCT, which allows accurate localization with no use of FMs. Although the image-guidance with CBCT can assure the precision and accuracy of patient position, radiation therapists need to take time to evaluate the image registration quality for correcting the patient's position.

To reduce the time required for decision-making, this paper proposes an image registration assessment method based on control chart monitoring. We first use control charts to quantify the variation of the registration similarity and we then monitor image registration scores to determine whether subsequent variations belong to special or common causes. More precisely, the planning CTs and daily CBCT images are registered using both cross-correlation and mutual information. For each patient, the registration scores are plotted for daily image registration, and

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patient-specific control limits are calculated. Control charts are then evaluated to identify out-of-control signals, and corresponding images are reviewed to find the cause of the out-of-control registration scores. Based on the control chart plotted by daily registration scores of each patient, the proposed method can detect both alignment errors and image quality inconsistency. Furthermore, the proposed method can provide users with a clear guideline to identify unacceptable image quality and unacceptable image registration under minimal effort. Experimental results demonstrate that by using control charts from a clinical database of 10 patients undergoing prostate radiotherapy, the proposed method can identify out-of-control signals and find special cause of out-of-control registration events.

2 Materials and Methods

2.1 Datasets

Ten patient prostate CT-sim datasets with 39 daily CBCT images constituted our dataset. These clinical images were acquired during radical prostate treatment by IMRT, with daily image guidance and repositioning correcting all setup errors. The patient images were gathered with Research Ethics Board (REB) approval.

2.2 Registration Measure

Mutual information (MI) and cross correlation (CC) are two of the most popular similarity measures used in image registration.^{21,22} MI is an information theory measure of the statistical dependence between two random variables and CC is a standard approach to feature detection between two images. Let 3-D images X and Y be the input images, and let x and y represent the corresponding voxel value of X and Y , respectively. The measure of mutual information between images X and Y is defined as

$$I(X, Y) = \sum_{x,y} p(x, y) [\ln[p(x, y)] - \ln(x) - \ln(y)], \quad (1)$$

where $p(x, y)$ is the joint probability distribution function of X and Y , and $p(x)$ and $p(y)$ are the marginal probability distribution functions of X and Y . The measure of cross correlation between images X and Y is given by

$$\begin{aligned} \text{Cov}(X, Y) &= E[X, Y] - E[X]E[Y] \\ &= \sum_{x,y} [p(x, y) - p(x)p(y)]xy, \end{aligned} \quad (2)$$

where $E[X]$ denotes the expectation of X and $E[X, Y]$ denotes the joint expectation of X and Y .

MI is often used in multimodality image registration but it may not provide the best accuracy in unimodality image registration. In comparison, CC is more suitable for unimodality image registration. Thus MI and CC may be viewed as good complements. In this study, both of them are used in image registration and quality assessment.

2.3 Image Preprocessing

2.3.1 Volume of interest

Daily CBCT images are registered to the planning CT images within a volume that extends in the craniocaudal direction from

the lumbo-sacral joint to inferior of the pubic bone; laterally around the pelvic rim, including femoral heads but excluding the femoral necks; and antero-posteriorly from the pubic bone to sacrum. To reduce computational costs, the image registration is performed within a clinically relevant region. The volume is manually selected by the operator at local hospital.

2.3.2 Image filtering

CT and CBCT images contain both negative and positive Hounsfield unit (HU) over a similar range. The same anatomy in the two images has different HUs, sometimes with opposite signs. For example, the prostate region in the CT image has a positive HU, but it has mostly negative HU in the CBCT image. Moreover, the HU of the CBCT image is not scaled in the same range as in CT. After the HU values are converted into pixel values suitable for registration, the different signs of corresponding pixels can cause the registration similarity measurements, especially cross-correlation, to be extremely low and therefore insensitive to describe the similarity between reference and guidance image. In our datasets, the region of interest surrounding the prostate is consistently positive in the CT-sim image and consistently negative in the CBCT image. Due to this feature, we used a simple projection technique by setting all negative HU values in the CT-sim image as zero and setting all positive HU values in the CBCT image as zero. Compared with standard normalization, the proposed filtering technique is able to preserve the local contrast of prostate while reducing the contribution of unwanted regions, such as bone and air. An example of filtered images is shown below in Fig. 1, whereas Figs. 1(a) and 1(c) are unfiltered CT and CBCT images, Figs. 1(b) and 1(d) are filtered CT and CBCT images, and the red boxes in CT-sim images in (a) and (b) represent the regions of interest. We can see that both the filtered CT and CBCT images have better contrast than the two unfiltered images in the regions of interest.

2.4 Statistical Process Control

2.4.1 Control charts

The most useful tool in statistical process control is the control chart. Control charts can be used to assist in decision-making and to provide a reliable way that maximizes the benefit of the complex and complicated technology required for adaptive radiotherapy. A control chart is a plot of measured properties of a process, which consists of a central line for the average of the process, and upper and lower control lines within the range of the process. In practice, the upper and lower control lines are chosen as 3 standard deviations (3σ) since the probability of normally distributed data point falling outside this range is 0.001.¹³

When the data are sampled from a process, we can plot its individual data value on a control chart. In this study, we use the similarity measure values (mutual information and cross-correlation) from daily image registration scores as our individual data. By plotting values of mutual information and cross-correlation for each pair of registered images, we can identify out-of-control cases prior to treatment.

2.4.2 Sampling requirement

For our study, we select control limits for quality inspection using a small set of data from the image registration process, and the control limits are used to identify out-of-control conditions during the remainder of the course of treatment. For each

Fig. 1 Comparison of CT-sim and CBCT image preprocessing. (a) and (c) Unfiltered CT and CBCT images, (b) and (d) filtered CT and CBCT images; red boxes plotted in (a) and (b) denote the regions of interest of two CT-sim images.

patient, we determine the control limits of the registration similarity using the first five measurements from patients' images without artifacts, and then we identify whether subsequent image registrations are in control or not. Usually, five supervised data points should be enough to establish a strong pattern for an in-controlled process. To ensure the correctness of the first five cases, the operator must examine both the guidance images and registration shifts, and determine if they are acceptable for an initial subset of daily image registration. If excess artifact or large positioning errors are observed, the daily similarity measure for image registration will not be included in the control limit calculation, and the measurements of the following treatment will be used until five acceptable samples are collected.

2.4.3 Control limits

Once the data are sampled, we are able to plot a control chart of the mean or standard deviation of each sample to produce so-called control charts. In this study, the upper and lower control limits for each patient are determined by¹³

$$\hat{x} \pm \frac{3\widehat{MR}}{1.128}, \quad (3)$$

where $\hat{x}$ is the mean, $\widehat{MR}$ is the average of the daily moving ranges of consecutive measurements, and the constant in the denominator is included because $\widehat{MR}$ is not an unbiased

estimator of the moving range of the data.⁸ Using the control limits, we can identify out-of-control conditions in subsequent registrations. Samples within the control limits will be considered in control, whereas samples out-of-the limits will indicate out-of-control behaviors and the presence of special causes.¹⁰

Remark: since daily CBCT images of a patient are registered to a single planning CT image, the trend of MI (or CC) values should maintain consistent over the period of treatment, as the similarities of the daily guidance images should be consistent with the reference image. As a result, we may determine an optimal control limit using the first five valid samples to describe the expected trend of registration similarities. Using control limits, we can judge which data point is in control or out of control, that is, which CBCT image is suitable for registration or not. Any image registration with a similarity value being outside the control limits will be considered as inconsistent.

2.5 Method Procedure

First, initial patient images are filtered to reduce artifacts in image registration. Second, the planning CTs and daily CBCT images are registered retrospectively using mutual information and cross correlation-based image registration algorithms. Third, daily image registration scores are plotted for each patient and specific control limits are calculated based on the first five image registrations. SPC control charts are then evaluated to identify out-of-control signals, and these image registrations

Fig. 2 Block diagram of proposed method procedure.

will be verified to find the cause of the out-of-control registration. Finally, once the assessed quality is acceptable, the treatment delivery will be performed. Figure 2 plots the block diagram of the proposed method procedure.

3 Results and Discussion

3.1 Control Charts

For the 10 patients, the center lines of the MI individuals control charts ranged from 0.15 to 0.3, and the center lines of the CC individuals control charts ranged from 0.2 to 0.4. The resulting metric values were plotted on control charts and out-of-control data points were identified. For example, Fig. 3 plotted individuals control charts for two patient data based on MI and CC. The control limits and center line (mean) were computed using the first five valid registration similarity measurements,

shown in solid red lines and solid black lines, respectively. The control charts were classified as “out of control” case and “in control” case. From Figs. 3(a) and 3(b), we see that most data points are within control limits, except for one outlier on day 25 displayed on MI individual chart and another outlier on day 15 displayed on CC individual chart, which are out of control. From Figs. 3(c) and 3(d), we see that all data points fall within the upper and lower control limits, which are in control.

3.2 Control Chart Verification

To identify image registration quality using control charts, Figs. 4–7 displayed control chart results of four patient data, respectively. Among these control charts, out-of-control and in control events were identified, and corresponding CBCT images were reviewed.

Fig. 3 Control charts of patient data 1 and 2. (a) and (c) under MI; (b) and (d) under CC. Thick solid lines indicate the mean; red lines are the upper and lower control limits.

Fig. 4 Example 1 for control chart results of patient data 3. (a) and (b) Control charts with MI and CC, (c) and (d) corresponding CBCT guidance images on day 8 and day 9, and (e) and (f) corresponding CBCT guidance images on day 16 and day 17.

3.2.1 Special causes

Based on out-of-control points in the control charts, a number of identified artifacts can be considered as the special causes.²³ They included anatomical deformation and unexpected contrast due to rectal gas; windmill artifact and motion blur caused by rectal gas motion; large anatomical changes since translation or deformation (or both) caused by rectum filling prevents reliable image registration; faulty image acquisition (partial arc, or

incomplete scan due to patient request or acquisition failure); and abnormal bladder contrast (residual iodinated IV contrast agent used in previous CT scans administered immediately prior to radiotherapy fractionation).

Figures 4(a) and 4(b) plotted the control charts of the first patient based on MI and CC measures, where two out-of-control cases on day 9 and day 17 were identified. According to this observation, we may conclude that the CBCT images corresponding to out-of-control cases are not suitable for image

Fig. 5 Example 2 for control chart results of patient data 4. (a) and (b) Control charts with MI and CC, (c) and (d) corresponding CBCT guidance images on day 14 and day 15, and (e) and (f) CBCT images of day 24 and day 25.

guidance due to unacceptable image quality. For qualitative validation, we compared the CBCT image on day 8 shown in Fig. 4(c) with the CBCT image on day 9 shown in Fig. 4(d). We observed that Fig. 4(d) has blurred contrast in region of interest due to the gas bubble in the rectum. Similarly, when comparing the CBCT image on day 16 shown in Fig. 4(e) with the CBCT image on day 17 shown in Fig. 4(f), we observed that Fig. 4(f) also has blurred contrast in region of interest. These artifacts may reduce the accuracy of image registration and cause misalignment between reference and guidance images.

Furthermore, we found that Figs. 4(c) and 4(e) had the residual prostate displacements being roughly <2 mm for in control cases, and Figs. 4(d) and 4(f) had the residual prostate displacements being roughly >4 mm for out-of-control cases. These analyses confirmed that by identifying out-of-control or in control cases we can determine whether the corresponding CBCT image is suitable for guidance.

In Fig. 5, we identify out-of-control causes on days 15 and 25. By comparing the images on day 14 and day 15, we observed that the gas bubble in rectum as shown in Fig. 5(d)

Fig. 6 Example 3 for control chart results of patient data 5. (a) and (b) Control charts with MI and CC, (c)–(g) corresponding CBCT guidance images on day 2, day 19, day 24, day 27, and day 29.

Fig. 7 Example 4 for results of the prostate displacement detected by control charts from patient data 6. (a) and (b) Control charts with MI and CC, (c) and (d) reference CT image and CBCT image on day 10, (e) registered image of both (c) and (d) with color overlay, and (f) registered image with prostate displacement.

has blurred contrast in region of interest once again. By comparing the images acquired on day 24 and day 25, we observed that Fig. 5(f) has extraordinary bladder contrast. This patient underwent a CT IV-contrast procedure before radiation therapy and the IV solution was still in the patient's bladder, causing extremely bright bladder contrast. Although the prostate displacement estimated here is under 2 mm, the abnormal bladder contrast would affect the registration quality, which is not suitable for image guidance.

In Fig. 6, multiple out-of-control events are observed between day 19 and day 39. For Figs. 6(d)–6(g), the estimated residual prostate displacements are 2, 5, 5, and 2 mm,

respectively. We found degradation in contrast and windmill artifact caused by the gas bubble in rectum. However, it is worth noting that the presence of a gas bubble alone may not be the special cause for out-of-control behavior as we observed in Fig. 6(a) on day 2. It is a special cause only when the presence of a gas bubble produces artifact, contrast degradation, and large anatomy deformation. Finally, the extreme outlier on day 39 is caused due to incomplete scan and it is easily identified on the control chart as well.

Finally, we have an example, shown in Fig. 7, to illustrate that the use of the SPC can easily identify the CBCT image with poor registration but it is difficult for the human

Fig. 8 Workflow of clinical image guidance.

observation to identify. Figures 7(a) and 7(b) are the control charts of the patient based on MI and CC measures. Figure 7(c) is the reference CT image, where the prostate region is delineated by a solid line and Fig. 7(d) is the CBCT image on day 10, where the prostate region is delineated by a dashed line. Figure 7(e) is the registered image with color overlay based on Figs. 7(c) and 7(d). From control chart shown in Fig. 7(a), we can easily detect out-of-control point on day 10 and thus we may conclude that the registered image shown in Fig. 7(e) has poor registration quality within the region of interest. Figure 7(f) confirmed that the registered image has residual prostate displacements being more than 5 mm. In contrast, it is difficult for the operator to determine whether the registered image has large prostate deformation solely based on visual inspection.

3.2.2 Common causes

Common cause accounts for the dispersions of the registration scores within the control limits from the center line. For example, small anatomical changes over the course of radiotherapy due to deformations, daily setup variation, and patient-weight changes, all contribute to the changes within control limits. Statistical noise can produce random thin bright and dark streaks. Random displacements of the image matrices of the images, coupled with partial volume effects, also produce common cause variation.

3.3 Application to Clinical Image Guidance

The SPC-based image guidance procedure is helpful for the successful implementation of adaptive radiotherapy. The use of

SPC for the evaluation of image registration has not been tested clinically. To achieve this, we introduce a clinical workflow of image guidance procedure using the proposed SPC assessment method. First, the planning CTs and daily image guidance cone beam CTs of patients undergoing prostate radiotherapy are retrieved from our clinical database. Those images are filtered to reduce artifacts in image registration. Second, the planning CTs and daily CBCT images are registered retrospectively using mutual information and cross-correlation methods. For each patient, the registration scores are plotted for each daily image registration, and patient-specific control limits are calculated based on the first five image registrations. Third, with a small number of fractions, there is a trade-off between the number of images used to set the control limits. After the control limits are set, each image registration is evaluated to determine whether the registration is in control. Control charts were then evaluated to identify out-of-control signals, and these image registrations are reviewed to try to find the cause of the out-of-control registration scores. Finally, once the image registration quality is acceptable, the treatment delivery proceeds. Figure 8 displays the workflow of clinical image guidance, based on the proposed assessment method.

It should be noted that if the registration is out of control, the therapist at the treatment unit has the following options. The therapist may determine that a valid registration and corrective shift are still possible. The therapist may elect to reimage to reduce artifacts or reposition the patient on the couch to compensate for a deficient image acquisition. In addition, the therapist may ask the patient to void their bladder or rectum for more accurate imaging.

4 Conclusion and Future Work

This paper has proposed an image registration assessment method based on SPC control chart monitoring. The application of SPC is helpful for assisting radiotherapists in assessment of image guidance quality. By monitoring image registration scores, the proposed assessment method can automatically identify unacceptable image quality and unacceptable image registration. Moreover, because the control chart is consisted of similarity measurement values between the reference CT image and daily CBCT image, the CBCT images corresponding to out-of-control cases will produce larger registration errors compared with the in control cases. Thus, the proposed method can provide a quick and reliable way to detect poor quality images and large alignment errors. In comparison with SPC assessment method using fiducial marker registration errors,¹⁴ our work can identify special causes for each out-of-control signal, which further validated the reliability of the proposed assessment method. Furthermore, the proposed assessment method can greatly reduce the user time, compared with traditional manual registration inspection. It allows operators to assess image registration quality with minimal effort. This is especially helpful for widespread clinical implementation for IGRT. Experimental results confirmed that using control charts from clinical database of 10 patients undergoing prostate radiotherapy, the proposed assessment method can identify out-of-control signals and find special cause of out-of-control registration events.

Other than prostate, the proposed assessment technique can also be used in IGRT for head and neck cancer, liver cancer, and lung cancer. Moreover, with the advancement of imaging and guidance technology, the proposed technique can be integrated

into many other related clinical applications. For example, the proposed assessment technique can be applied to MR-guided radiotherapy, where there is a greater potential for image guidance errors due to the multitude of MR image types. Furthermore, image guidance is the enabling technology of adaptive radiotherapy, and the delivery of adaptive image-guided IMRT will benefit from automated decision aids to assess the quality of image registration. Further applications of the proposed assessment technique will be verified on a larger scale. These issues will be the focus of our research in the future.

Disclosures

The authors declare no conflicts of interest in relation to the work in this paper. The REB number of this study is 15-8730.

Acknowledgments

Ontario Consortium for Adaptive Interventions in Radiation Oncology (OCAIRO) is grateful for funding from the Ontario Research Fund for the research toward developing robust hardware, software, imaging and database systems that will advance effective and innovative adaptive radiation therapy methods to the clinical setting while establishing Ontario as a global leader in adaptive interventions in radiation oncology. The authors also thank the associate editor and reviewers for their encouragement and valuable comments, which helped in improving the quality of the paper.

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