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PHYSICS CONTRIBUTION

MULTIMODALITY IMAGE REGISTRATION QUALITY ASSURANCE FOR CONFORMAL THREE-DIMENSIONAL TREATMENT PLANNING

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Purpose: We present a quality assurance methodology to determine the accuracy of multimodality image registration and fusion for the purpose of conformal three-dimensional and intensity-modulated radiation therapy treatment planning. Registration and fusion accuracy between any combination of computed tomography (CT), magnetic resonance (MR), and positron emission computed tomography (PET) imaging studies can be evaluated.

Methods and Materials: A commercial anthropomorphic head phantom filled with water and containing CT, MR, and PET visible targets was modified to evaluate the accuracy of multimodality image registration and fusion software. For MR and PET imaging, the water inside the phantom was doped with $CuNO_3$ and ^{18}F-fluorodeoxyglucose (^{18}F-FDG), respectively. Targets consisting of plastic spheres and pins were distributed throughout the cranium section of the phantom. Each target sphere had a conical-shaped bore with its apex at the center of the sphere. The pins had a conical extension or indentation at the free end. The contours of the spheres, sphere centers, and pin tips were used as anatomic landmark models for image registration, which was performed using affine coordinate-transformation tools provided in a commercial multimodality image registration/fusion software package. Four sets of phantom image studies were obtained: primary CT, secondary CT with different phantom immobilization, MR, and PET study. A novel CT, MR, and PET external fiducial marking system was also tested.

Results: The registration of CT/CT, CT/MR, and CT/PET images allowed correlation of anatomic landmarks to within 2 mm, verifying the accuracy of the registration software and spatial fidelity of the four multimodality image sets.

Conclusions: This straightforward phantom-based quality assurance of the image registration and fusion process can be used in a routine clinical setting or for providing a working image set for development of the image registration and fusion process and new software. **© 2001 Elsevier Science Inc.**

Image registration, Image fusion, Treatment planning.

INTRODUCTION

Spatially accurate medical images are an essential tool in three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT) treatment planning (1). Kilovoltage X-ray computed tomography (CT) imaging is the current standard modality for image-based radiation therapy treatment planning, because of its high spatial resolution and fidelity. CT imaging studies are registered via laser-defined patient setup fiducial marks and used to define anatomic structures and target volumes from which beam shapes and orientations are planned (1–9). When properly calibrated and free of image artifacts, CT images can provide electron density information for heterogeneity-based dose calculations. The major weakness of CT imaging is its limited soft tissue contrast.

Imaging modalities other than CT are useful in accurately delineating tumor volumes (10–12). Magnetic resonance imaging (MRI), magnetic resonance spectroscopy, single photon emission computed tomography (SPECT), and positron emission tomography (PET) are imaging modalities that can provide unique target information and may improve overall radiation therapy patient management (13–15). All of these imaging modalities provide valuable forms of treatment planning information that complement each other.

MRI provides excellent soft tissue contrast, which allows better differentiation between normal tissues and many tu-

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mors. Magnetic resonance spectroscopy promises to extend this contrast to the metabolic and biochemical level. Additionally, MRI is not limited to axial plane image acquisition. Disadvantages of MRI include susceptibility to spatial distortion and image intensity values that are not easily translated into electron density values. Spatial distortion may alter position of target volumes with respect to other anatomic landmarks, patient skin, or external fiducial markers, rendering an MRI study unsuitable for treatment planning.

SPECT and PET also provide unique information about patient physiology rather than anatomy. These modalities have been used for evaluation of tumor metabolism, differentiation between tumor recurrence and radiation necrosis, evaluation of regional lung function, detection of hypoxic areas of the tumor, and other functional imaging. Limitations of PET and SPECT imaging include poor spatial resolution, which may lead to inaccurate delineation of external patient contours and other normal structures.

When multiple imaging studies are employed, they must be spatially registered to accurately aid in tumor volume delineation. Registration of multimodality images is a several-step process requiring multifunction software capable of image set transfer, storage, coordinate transformation, and voxel interpolation. These features enable image study registration (transforming images to a common reference frame and resampling to a common pixel grid) and fusion (the display of a combination of pixel intensities from registered image studies). Registered and "fused" image studies can then be used for 3D-CRT and IMRT treatment planning. The image registration process is prone to errors that can in turn cause serious patient treatment errors. Because of this, quality assurance (QA) of the image registration process is essential for the verification of post-transfer image data integrity, image spatial integrity, image orientation, image chirality (i.e., absence of image mirroring), image registration accuracy, and other system functionality.

As outlined in the American Association of Physicists in Medicine Task Group 53 Report (16), general commissioning and routine procedural quality assurance checks of a multimodality image registration process used for treatment planning are recommended. The task group report also acknowledged that multimodality image registration is a "large and complex area" requiring further development and meriting its own task group report. This study provides a limited but important step toward that end, namely the development of a straightforward method for performing CT, magnetic resonance (MR), and PET quality assurance checks of image registration.

METHODS AND MATERIALS

A multimodality image registration QA phantom must contain structures visible on all imaging modalities that are being evaluated. A commercially available phantom (RSVP

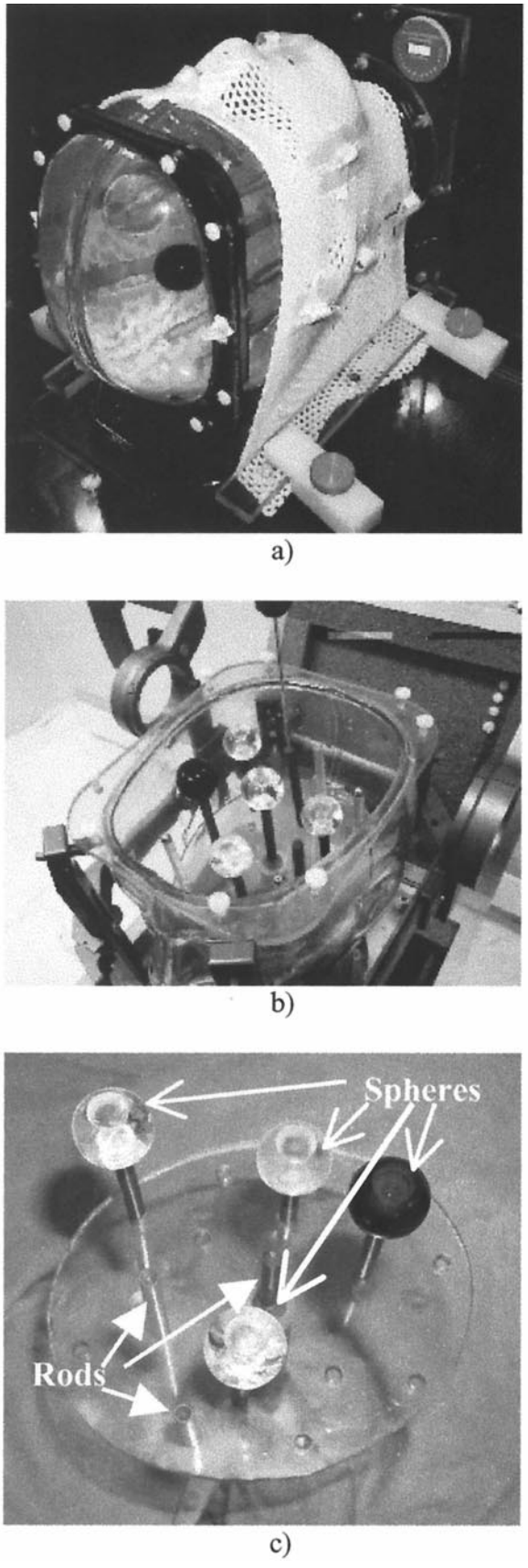

Fig. 1. (a) Imaging phantom immobilized with thermoplastic mask. (b) Phantom with top section removed. (c) Target holder removed from the phantom, showing spheres and rods.

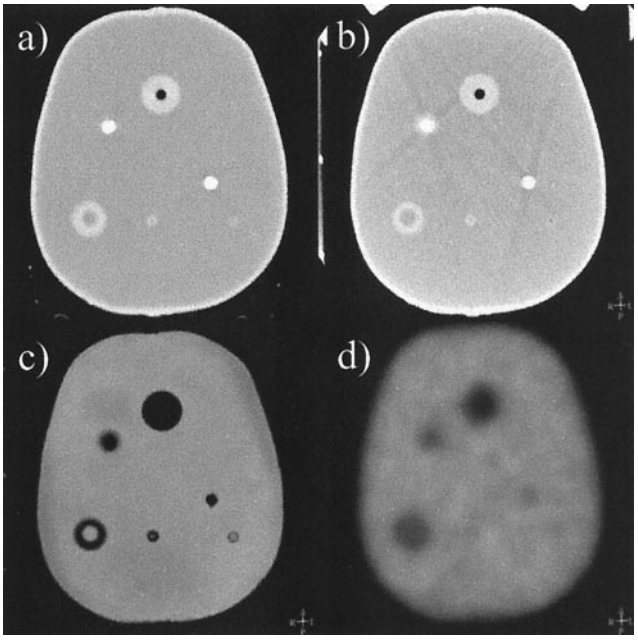

Fig. 2. (a) Primary CT. (b) Second CT. (c) MRI. (d) PET images taken with phantom in Fig. 1.

Phantom, The Phantom Laboratory, Salem, NY) was modified for evaluation and verification of the registration process. The commercial phantom is a plastic anthropomorphic head of average human size (Fig. 1), initially developed for assessment of stereotactic localization accuracy in stereotactic ring-based brain surgery (13, 17). Plastic spheres and rods were strategically placed throughout the cranium section of the phantom. The superior end of the phantom can be opened at a watertight gasket seal to provide access to target

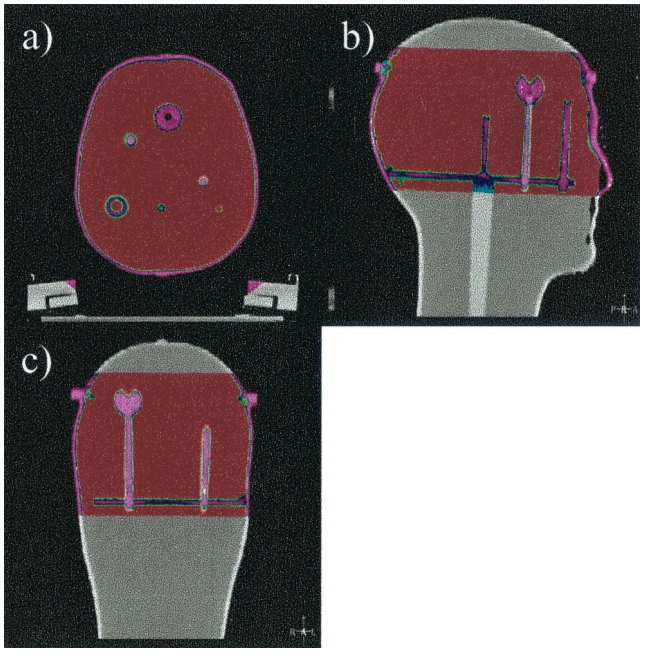

Fig. 3. Grayscale primary CT scan with overlaid colorwash MRI scan. (a) Axial, (b) Sagittal, and (c) Coronal views.

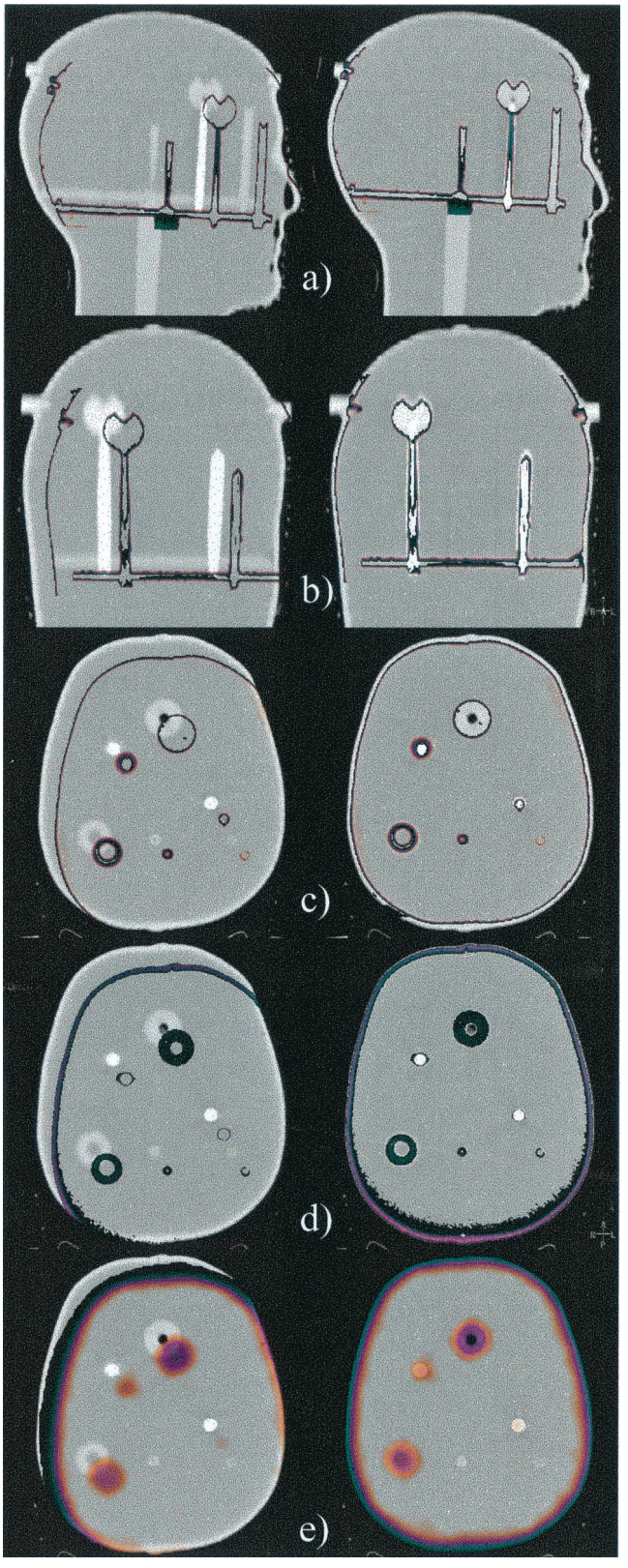

Fig. 4. Examples of planar coregistration images showing offset (left) and aligned (right) image data sets. (a) Grayscale sagittal primary CT image with colorwash of second CT scan overlaid. (b) Coronal primary CT image with the second CT scan overlaid. (c–e) Grayscale axial primary CT image with overlaid colorwash of second CT scan, MRI scan, and PET scan, respectively.

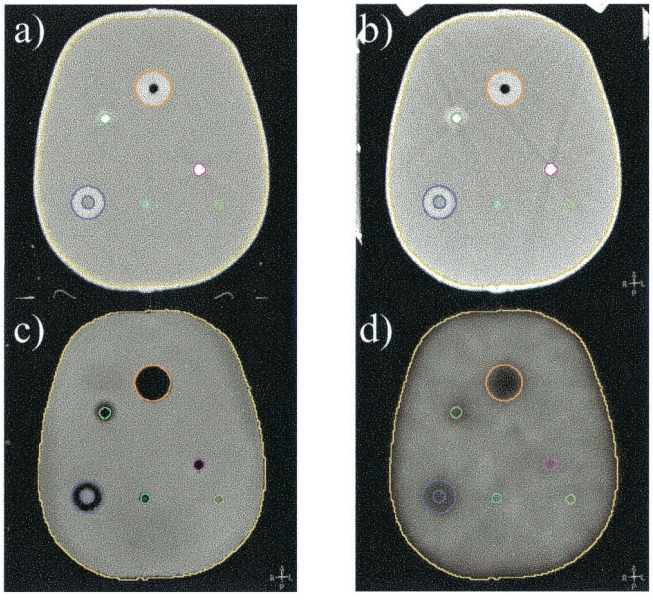

Fig. 5. (a) Primary CT with contoured spheres and rods. (b–d) Second CT, MRI, and PET with overlaid primary CT contours, respectively. The inner circle of the two concentric contours is an outline of the inner cone-shaped bore.

objects. Target spheres of 25.4 mm in diameter were threaded onto plastic posts. Each sphere had a conical bore with its apex at the center of the sphere. For MRI and PET imaging, the water inside the phantom was doped with $CuNO_3$ and ^{18}F-FDG, respectively. Tap water was used for CT imaging. The conical indentations on spheres and rods, as well as the points on rods, were visible objects with all three imaging modalities, satisfying the primary phantom objective.

Four sets of the phantom images were obtained: (*1*) primary CT scan of a phantom immobilized with a thermoplastic mask, (*2*) a second CT scan on a different scanner for evaluation of CT/CT image fusion of the phantom immobilized with a stereotactic ring, (*3*) an MR scan of the phantom immobilized with a stereotactic ring, and (*4*) a PET scan of a phantom immobilized with a thermoplastic mask (Fig. 2). Three different image registrations were evaluated: primary CT to second CT, primary CT to MR, and primary CT to PET. Different immobilization methods were specific to respective scanners.

The image registration was performed using a commercially available treatment simulation system (ACQSIM Oncodiagnostic Simulation/Localization System, Marconi Medical Systems, Inc., Cleveland, OH). The software has the capability of reconstructing axial images from volumetric CT, MR, and PET image studies in arbitrary planes. For image registration, axial, sagittal, and coronal images were used (Fig. 3).

Multimodality image registration can be performed with the software system using external patient (phantom) contours: The computer performs registration without user interaction. Two registration methods requiring user interaction are point matching (a minimum of three common points are selected on both sets of images registered), and interactive image-based registration (a color wash of one image set is displayed over a grayscale image of the other set) (Fig. 4). In Fig. 4, images on the left side were taken before registration; images on the right were taken after alignment.

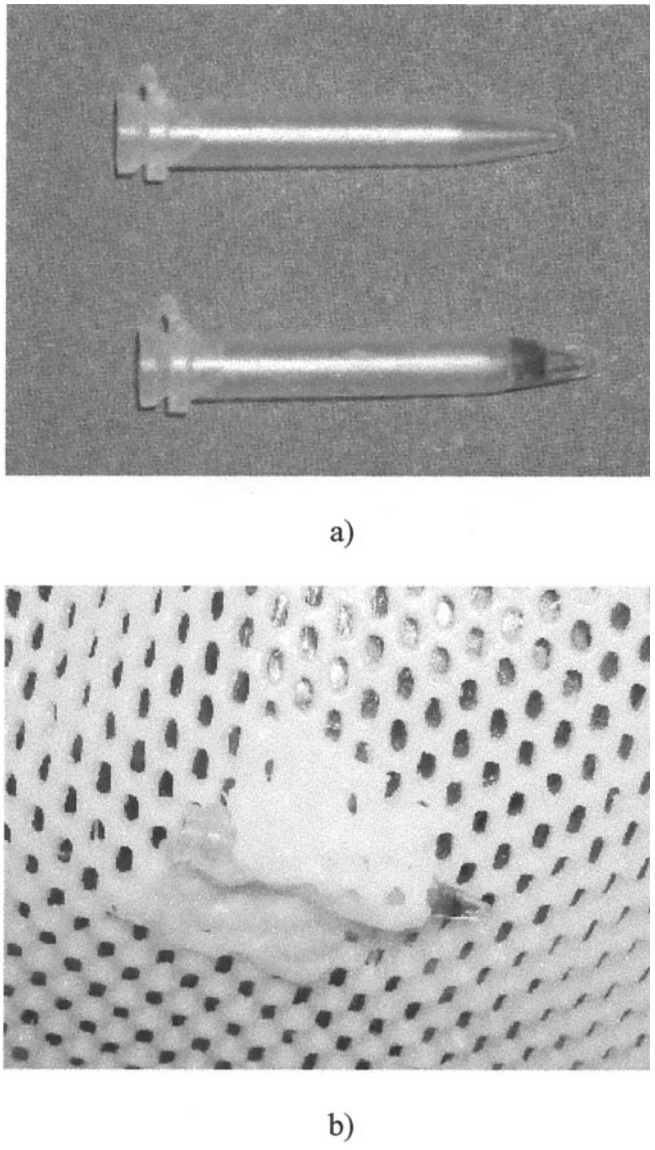

Fig. 6. (a) Plastic ampoules that serve as fiducial markers. (b) Marker attached to thermoplastic mask.

The interactive registration method was used for registration of all four sets of images. Registration was performed on the three major axes until a satisfactory alignment was obtained. Figure 5a shows the primary CT with contoured spheres and rods. Figures 5b–d show, respectively, the second CT, MRI, and PET after registration with overlaid primary CT contours.

A set of novel fiducial markers designed for clinical use was employed to assist in image registration verification of PET images to the primary CT set (Fig. 6). The markers are also MR compatible. The fiducial markers were made with disposable plastic microcentrifuge tubes (VWRbrand Disposable Microcentrifuge Tubes, VWR Scientific Products, West Chester, PA) that were 0.5 cm in diameter, 3.5 cm

long, and 0.25 ml, commonly found in chemistry and biology laboratories. One end of the ampoules is conical, and the other end can be opened and closed with a small cap. For CT scans, two small pieces of aluminum wire were placed at the pointed end of the ampoules and secured in place with dental wax. The bottom ampoule shown in Fig. 6a has two aluminum wires at the tip and dental wax in place to hold the wires. For PET scans, a small drop of ^{18}F-FDG is placed at the pointed end of the fiducial marker. The drop is held in place by the liquid surface tension. The surface tension is strong enough that the fiducial marker can be handled without worry that the drop may be displaced. Also for PET scans, the radioactive material is safely contained in the plastic ampoules. For MR scans, a small drop of $CuNO_3$ solution can be placed at the tip of the pointed end. The markers were rigidly and reproducibly attached to the thermoplastic mask using a small piece of thermoplastic material, allowing easy replacement between different imaging modality scans (Fig. 6b).

RESULTS

Image registration was verified by manually comparing identified sphere and rod centroids on the primary CT study to centroids identified in the second CT scan, MR, or PET image studies (Fig. 5). Table 1 shows the maximum and standard deviations of sphere centroid locations relative to the primary CT in three dimensions, as identified on the other three image studies. The 2σ standard deviations of all registered centroids were within 2.0 mm in each dimension from their expected locations on the second CT, MR, and PET scans. A study of reproducibility (10 blind centroid identifications) gave a standard deviation of 0.2 mm. Registration accuracy was also verified by observing locations of fiducial markers on the primary CT and PET image studies. The fiducial markers were outlined on the primary CT scan and compared with their observed locations on PET images. This method of registration reproduced the alignments within 2 mm of agreement. This is an excellent agreement considering 2.57 mm^3 isotropic PET study voxels.

Table 1. Maximum and standard deviations of CT-CT, CT-MR, and CT-PET image registrations

Sphere ID	x_{max} (mm)	y_{max} (mm)	z_{max} (mm)	x_σ (mm)	y_σ (mm)	z_σ (mm)
1	0.73	0.86	1.30	0.42	0.38	0.82
2	1.42	0.86	2.53	0.42	0.35	1.06
3	1.23	0.81	1.23	0.56	0.30	1.00
All	1.42	0.86	2.53	0.58	0.37	0.90

DISCUSSION AND CONCLUSIONS

With careful manual registration, the surfaces of spheres and rods from the primary CT scan were found to closely match the corresponding features in other image studies. The novel thermoplastic mask–mounted fiducial markers were found to provide equally acceptable results. This QA procedure is easily reproduced and will be performed on an annual basis or on the introduction of any new scanner or software revision.

Multimodality imaging is increasingly used to define the spatial extent of many tumor sites. Radiation therapy target delineation is rapidly becoming dependent on imaging modalities other than CT. The number of treatment planning systems that support image registration and fusion is growing to meet this demand. Thus, there exists a need to perform periodic QA of the overall image fusion process. This QA process is essential and should evaluate image integrity after data transfer, chirality, image spatial integrity, image fusion accuracy, and the overall system functionality. Fusion inaccuracies and image study problems can be demonstrated in multiple ways. Simple misregistration could appear, as on the left side of Fig. 4. Image mirroring in one of the fusion studies would result in target objects appearing on opposite sides in two studies. Problems with image spatial integrity and distortion would be revealed by inability to align all of the spheres between two image studies. Failures in these functionalities have the potential to cause catastrophic treatment errors. The QA process should demonstrate that the overall fusion accuracy is within an acceptable tolerance for 3D-CRT or IMRT treatment planning (2–5 mm) (16). In this study, the registrations performed between CT, MR, and PET were accurate to within 2 mm.

REFERENCES

1. Purdy JA. 3D treatment planning and intensity-modulated radiation therapy. *Oncology* 1999;13(Suppl. 5):155–168.
2. Goitein M, Abrams M. Multi-dimensional treatment planning: Beam's eye-view, back projection, and projection through CT sections. *Int J Radiat Oncol Biol Phys* 1983;9:789–797.
3. Cheng CW, Chin LM, Kijewski PK. A coordinate transfer of anatomical information from CT to treatment simulation. *Int J Radiat Oncol Biol Phys* 1987;13(10):1559–1569.
4. Michalski JM, Purdy JA, Harms W, Matthews JW. The CT-simulation 3-D treatment planning process. *Front Radiat Ther Oncol* 1996;29:43–56.
5. Nishidai T, Nagata Y, Takahashi M, *et al*. CT simulator: A new 3-D planning and simulating system for radiotherapy: Part 1. Description of system. *Int J Radiat Oncol Biol Phys* 1990;18(3):499–504.
6. Perez C, Purdy J, Harms W, *et al*. Design of a fully integrated three-dimensional computed tomography simulator and preliminary clinical evaluation. *Int J Radiat Oncol Biol Phys* 1994;30:887–897.
7. Ragan D, He T, Mesina C, Ratanatharathorn W. CT based simulation with laser patient marking. *Med Phys* 1993;20:379–380.
8. Sherouse G, Bourland J, Reynolds K, McMurray H, Mitchel T, Chaney E. Virtual simulation in the clinical setting: Some

practical considerations. *Int J Radiat Oncol Biol Phys* 1990; 19:1059–1065.
9. Sherouse G, Chaney E. The portable virtual simulator. *Int J Radiat Oncol Biol Phys* 1991;21:475–482.
10. Torre W, Garcia-Velloso M, Galbis J, Fernandez O, Richter J. FDG-PET detection of primary lung cancer in a patient with an isolated cerebral metastasis. *J Cardiovasc Surg (Torino)* 2000;41(3):503–505.
11. Slevin N, Collins C, Hastings D, *et al*. The diagnostic value of positron emission tomography (PET) with radiolabelled fluorodeoxyglucose (18F-FDG) in head and neck cancer. *J Laryngol Otol* 1999;113(6):548–554.
12. Nowak B, Martino ED, Janicke S, *et al*. Diagnostic evaluation of malignant head and neck cancer by F-18-FDG PET compared to CT/MRI. *Nuklearmedizin* 1999;38(8):312–318.
13. Chao K, Bosch W, Mutic S, *et al*. A novel approach to overcome hypoxic tumor resistance: ATSM guided intensity modulated radiation therapy. *Int J Radiat Oncol Biol Phys* 2001;49(4):1171–1182.
14. Ling C, Humm J, Larson S, *et al*. Towards multidimensional radiotherapy (MD-CRT): Biological imaging and biological conformality. *Int J Radiat Oncol Biol Phys* 2000;47:551–560.
15. Kessler ML, Pitluck S, Petti P, Castro JR. Integration of multimodality data for radiotherapy treatment planning. *Int J Radiat Oncol Biol Phys* 1991;21(6):1663–1667.
16. Fraass B, Doppke K, Hunt M, *et al*. American Association of Physicists in Medicine Radiation Therapy Committee Task Group 53. Quality assurance for clinical radiotherapy treatment planning. *Med Phys* 1998;25(10):1773–1829.
17. Drzymala R, Mutic S. Stereotactic imaging quality assurance using an anthropomorphic phantom. *Comp Aid Surg* 1999;4: 248–255.