Registration of Three-Dimensional MR and CT Studies of the Cervical Spine

Ashok Panigrahy, Shelton D. Caruthers, Jaroslaw Krejza, Patrick D. Barnes, Sami G. Faddoul, Lynn A. Sleeper and Elias R. Melhem

AJNR Am J Neuroradiol 2000, 21 (2) 282-289
http://www.ajnr.org/content/21/2/282

AJNR Am J Neuroradiol 21:282–289, February 2000

Technical Note

Registration of Three-Dimensional MR and CT Studies of the Cervical Spine

Ashok Panigrahy, Shelton D. Caruthers, Jaroslaw Krejza, Patrick D. Barnes, Sami G. Faddoul, Lynn A. Sleeper, and Elias R. Melhem

Summary: A three-dimensional image registration technique for CT and MR studies of the cervical spine was evaluated for feasibility and efficacy. Registration by means of external fiducial markers was slightly more accurate than registration by anatomic landmarks. The interrelationships between bony (eg, neural foramina) and soft tissue structures (eg, nerve roots) in the cervical spine were more conspicuous on registered images than on conventional displays. Registration of CT and MR images may be used to examine more precisely the relationships between bony and soft tissue structures of the cervical spine.

In clinical practice, multitechnique imaging is not routinely done. In complex cases, however, data obtained from different imaging techniques may be complementary and provide useful anatomic and functional information that has repercussions for clinical treatment and management. Recently, imaging workstations have been used to register and display fused images in which the corresponding findings from two or more techniques are combined into a single image. Previous studies have shown that fused images represent a significant improvement over conventional images for depicting the relationship between bone and soft tissue (1–4). For example, registered MR images and CT scans of the head have been used by Hill et al (1) for planning skull base surgery and frameless stereotactic neurosurgery, and for staging nasopharyngeal carcinoma.

One region in which image registration would be potentially useful is the cervical spine. The bony elements of the cervical spine are best delineated by CT, while MR imaging provides superior delineation of the soft tissue elements. In the evaluation of bony degenerative disease or traumatic injury for possible spinal cord or nerve root compression, it would be ideal to combine CT scans and MR images. The main goal of this study was to test the hypothesis that fused displays of CT and MR studies of the cervical spine in healthy subjects would depict interrelationships of bony and soft tissue structures better than conventional displays. Our second goal was to test the hypothesis that the use of fiducial landmarks in the cervical spine would yield more accurate registration than would anatomic landmarks.

Received March 18, 1999; accepted after revision August 27.

From the Department of Radiology, Boston Medical Center, Boston, MA (A.P., S.D.C., J.K., S.G.F., E.R.M.); the Department of Radiology, Children's Hospital, Boston, MA (A.P., P.D.B.); Philips Medical Systems, N.A., Shelton, CT (S.D.C.); and New England Research Institutes, Watertown, MA (L.A.S.).

Address reprint requests to Elias R. Melhem, MD, Department of Radiology, The Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287.

Technique

Image Acquisition

Eight multitechnique radiologic markers (IZI Corp, Baltimore, MD) were attached to the skin of the neck of 10 volunteers (six men and four women, 25–42 years old) with no known neurologic problems. The markers, made of a polymer (hydrogel with 0.4% iodine) that is easily seen on both CT scans and MR images, were taped to the skin by adhesive glue and positioned such that not all of them were coplanar. Each volunteer was fitted with a neck brace to ensure consistent positioning of the neck during both imaging procedures. General institutional review board approval was obtained for this study and informed consent was obtained from all participating volunteers.

Spiral CT scans were acquired first with 512 × 512 pixels, a field of view of 240 mm, a section thickness of 3 mm, a pitch of 1.25, and an index of 2. MR images were then acquired using a 1.5-T system. A three-dimensional (3D) image volume was acquired using a turbo spin-echo sequence in a multislab fashion (10 slabs). From the data, 100 sections, each 1.5-mm-thick, were reconstructed. The matrix was 256 × 218 and covered a field of view of 230 × 230 mm. Other imaging parameters were TR/TE = 2500/100, flip angle = 90°, turbo factor (or echo train length) = 13, echo spacing = 14.3 milliseconds, and total scan time = 14 minutes. The images were acquired with the subjects lying supine on the flat portion of a multielement phased-array surface spine coil operating in the receive mode. Scout projection images from the CT examination were used to position the subjects for the subsequent MR examination. For processing, the image data were transferred via direct digital network from the CT and MR systems to an EasyVision workstation (software release 2.1.2, Philips Medical Systems, Shelton, CT).

Point-Based Registration

The first part of the registration procedure consisted of identifying landmarks on each type of image (CT or MR) corresponding to either the anatomic landmarks (Table 1) or the strategically placed fiducial markers (Fig 1). The unregistered MR and CT images were displayed as sequences of two-dimensional (2D) sections on which the user identified the 3D coordinates of the equivalent external markers and anatomic features. Figure 1 shows the location of the external fiducials

TABLE 1: Anatomic landmarks used for registration of MR images and CT scans

Anatomic Landmark	Geometric Description*
Anterior edge of odontoid process	Maximum edge of a curved surface
Right transverse foramina of C2	Intersection of a line and a surface
Left transverse foramina of C2	Intersection of a line and a surface
Lateral end of right lamina of C3	End of a line
Lateral end of left lamina of C3	End of a line
Medial end of right pedicle of C5	End of a line
Medial end of left pedicle of C5	End of a line
Tip of spinous process of C7	Junction of a line with a surface

* Based on geometric descriptions from Hill et al (1).

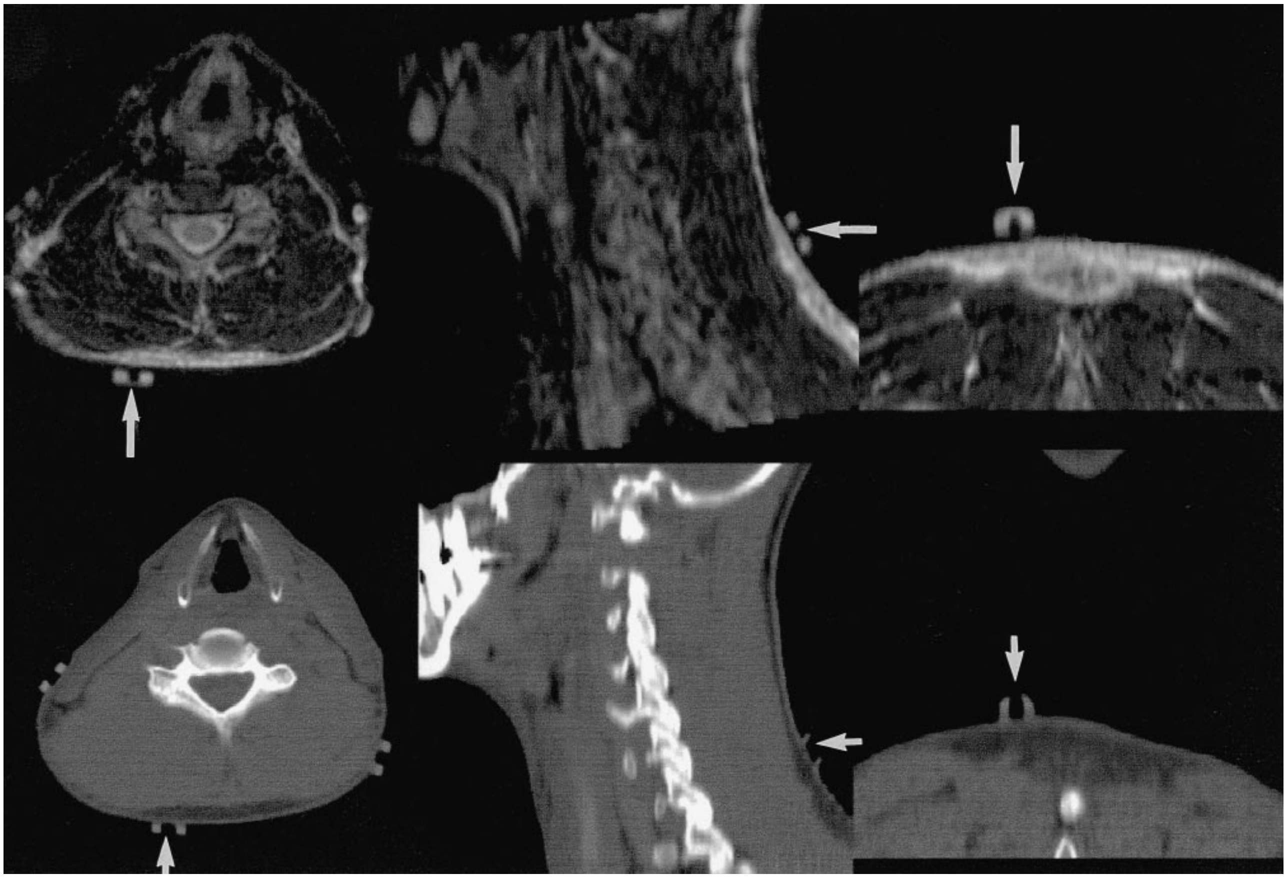

FIG 1. Location of external fiducials on orthogonal CT scans and MR images at a comparable level of the cervical spine. The external fiducial landmark (*arrows*) is first located on the axial view of the individual imaging studies and then compared with the location on the reformatted sagittal and coronal sections through the image volume.

on corresponding CT and MR studies at one level of the cervical spine. The external fiducial was first located on the axial views of the CT and MR images individually and then compared on the corresponding reformatted sagittal and coronal views. (Each corresponding fiducial was tagged with the same landmark name before the registration process was initiated.)

In the second part of the procedure, the software was used to register the CT and MR data sets via translation, rotation, and scaling (ie, with nine degrees of freedom). The 3D coordinates of the selected points were used to determine the coordinate transformation relating the MR and CT images. This step is achieved using a least squares fitting algorithm. The registration algorithm, which has been previously described in detail by Hill et al and others (1–5), assumes that the images acquired are related by a 3D rigid body transformation. The transformation is determined from the landmarks identified above. The translation and rotation components of the transformation are determined separately: the translation component is determined by aligning the centroids of the identified landmarks, and the rotational component is determined by using the method of singular value decomposition to find the three orthogonal rotations that minimize the sum of the squares of the displacements between corresponding registered landmark locations. After the least square fit, the residual displacement between corresponding landmarks is considered the registration error. A minimum of three noncolinear landmarks is required for image registration. The accuracy of registration increases with the number of landmarks identified and with the dispersion of the landmarks to the periphery of the data set.

The registration algorithm calculates the registration error for each of the point landmarks and the root mean square error (RMSE) for all points. The RMSE is calculated by dividing

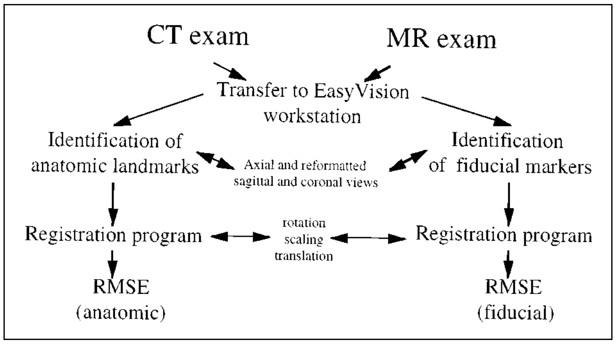

FIG 2. Diagram of the registration process.

the summed squared errors by the number of landmark pairs, and then taking the square root. The registration process was performed twice for each subject, once using the eight fiducial markers as landmark points and a second time using eight anatomic landmarks (Table 1). A summary of the registration process is diagramed in Figure 2. An RMSE value was calculated for each type of registration. The resulting registration was evaluated by viewing the fused images in any of a number of ways supported by the user interface. These included overlaid displays (with optional thresholds) and "curtain-view" shutter-type displays. For each subject, reformatted midsagittal images of the fused reconstruction performed with the fiducial markers were used to evaluate the anatomic alignment of the cervical spine. The alignment of the cervical spine for each subject was rated as satisfactory or unsatisfactory depending on differing angles of extension or flexion between the CT and MR examinations. MR image resolution (ie, identification of all eight external fiducial markers) was also rated as satisfactory or unsatisfactory. Results were tabulated with the corresponding fiducial landmark RMSE value.

To assess the quality of the fused images for clinical use, three neuroradiologists evaluated the fused images. For this analysis, corresponding MR, CT, and fused MR/CT axial images were generated and placed side by side on film for six corresponding levels of the cervical spine (approximately at the level of the neural foramina) for each subject. Registration of these images was performed by using external fiducial markers. Only eight subjects were used for the analysis. Two cases were excluded from quality assessment owing to protocol violation (use of a different coil, which resulted in excessive neck extension) and motion artifacts (resulting in poor image resolution and the inability to locate all eight external fiducial markers). The criteria (Table 2) used for the evaluation were 1) conspicuity of the vertebral body, 2) conspicuity of the posterior elements (cancellous versus noncancellous), 3) conspicuity of the relationship between the margins of the neural foramen and its contents, 4) conspicuity of the contents of the neural foramina, 5) conspicuity of the relationship between the margins of the spinal canal and its contents, and 6) conspicuity of the contents of the spinal canal. The conspicuity of the images was graded independently by three assessors on a three-point scale: -1 = less conspicuous than the conventional display, 0 = as conspicuous as the conventional display, $+1$ = more conspicuous than the conventional display.

Statistical Methods

The statistical difference between the RMSEs of the fiducial and anatomic landmark registrations was determined by the Wilcoxon signed rank test. Two subjects were excluded from image quality assessment after determining that their RMSE values were statistical outliers relative to a χ^2 distribution with nine degrees of freedom. These two subjects were also excluded because of protocol violations and motion artifacts (see above). For the clinical application analysis, the significance of any change in conspicuity between the conventional display and the registered image was tested by using the binomial sign test (6). That is, all scores of zero were ignored, and all positive and negative scores were summed for all subjects and for all three assessors for each criterion. The significance of any difference between the number of positive and negative scores was tested using the binomial distribution.

Because the data set contained correlated observations (ie, each of three assessors assigned scores to the same subject's image), a random effects model accounting for the correlation among the observations within each subject was considered the most appropriate statistical method for analyzing these data. However, the small sample size and low variability of the scores resulted in numerical instabilities, which prevented the random effects model from being estimated. Therefore, the binomial sign test results were used with a lower significance level (type I error rate of .01) to compensate for the fact that the binomial sign test, which assumes that all observations are independent (uncorrelated), will usually produce smaller P values than will a correlated data analysis applied to this study design.

Results

Correlation of Fiducial Landmark RMSE with Image Resolution and Alignment of the Cervical Spine

The RMSE values for each of the registrations using external fiducial markers for the 10 subjects ranged from 1.5 to 6.2 mm (1.5, 2.1, 1.5, 1.9, 1.9, 1.5, 1.5, 1.4, 6.2, and 5.8 mm). The MR images for the subject whose RMSE value was equal to 6.2 mm showed poor resolution because of motion artifacts, making it difficult to locate all eight external fiducial markers on these studies. In the subject whose RMSE was equal to 5.8 mm, there was poor anatomic alignment of the cervical spine between the CT scan and comparable MR image owing to excessive neck extension caused by use of a different coil. These subjects had the highest RMSE values in the data set, and these values were considered highly unlikely to be observed by chance; that is, within the limits of random variation ($P < .0001$). These two cases were excluded from further analysis on the basis of this statistical probability and for violation of protocol. An RMSE value less than 2.1 mm was consistent with both satisfactory image resolution and satisfactory alignment of the cervical spine.

Comparison of Accuracy between the Anatomic and Fiducial Marker Registration

The RMSE of registration based on external markers was 35% less than the RMSE based on anatomic features (Wilcoxon sign rank test, P value = .016) (Fig 3A). The range of RMSE values calculated for registration using external fiducial markers was 1.4 to 2.1 mm, whereas the RMSE range for anatomic registration was 4.1 to 2.0 mm (Fig 3B). Of note, subject 2 had identical RMSE values (2.1 mm) for both fiducial and anatomic registration (Fig 3B).

TABLE 2: Conspicuity of fused images compared with conventional display (*P* value < .01 considered significant)

Criteria	Reader No.	Subject No. 1	2	3	4	5	6	7	8	Total Positive Findings	Total Negative Findings	*P* Value
Conspicuity	1	−1	+1	+1	0	+1	−1	−1	+1			
of the vertebral	2	−1	+1	+1	0	+1	+1	−1	+1	15	5	.0414
body	3	+1	+1	+1	0	+1	0	+1	+1			
Conspicuity	1	−1	−1	+1	+1	−1	+1	+1	−1			
of the posterior	2	−1	−1	+1	+1	0	+1	0	+1	14	7	.1892
elements	3	−1	+1	+1	+1	+1	+1	0	+1			
Conspicuity of the relation-	1	+1	+1	+1	0	0	+1	+1	+1			
ship between margins of neural	2	+1	+1	+1	−1	0	+1	+1	+1	18	1	.00008
foramina and contents	3	+1	+1	+1	+1	0	0	+1	+1			
Conspicuity	1	0	−1	−1	−1	0	0	0	0			
of contents of	2	+1	+1	−1	−1	0	+1	0	0	4	6	.7539
neural foramina	3	0	0	−1	0	0	0	0	+1			
Conspicuity of the relation-	1	0	+1	+1	0	+1	+1	+1	+1			
ship between margins of	2	+1	0	0	−1	0	0	0	+1	14	1	.00098
spinal canal and contents	3	0	0	+1	+1	+1	+1	+1	+1			
Conspicuity	1	0	0	−1	−1	0	0	0	0			
of contents	2	0	+1	0	0	0	+1	+1	+1	7	2	.1797
of spinal canal	3	0	0	0	0	0	+1	+1	+1			

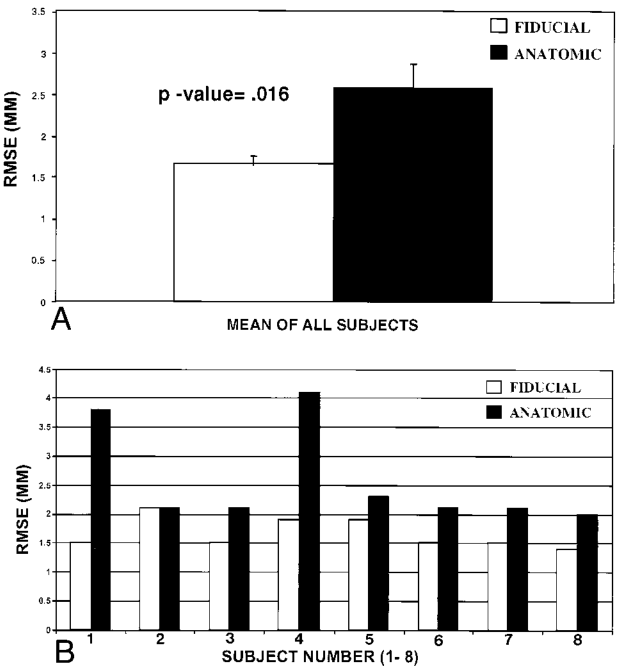

FIG 3. *A,* Bar graph shows that the RMSE value of the fiducial registration in all eight subjects is less than that of the anatomic registration (error bars represent SEM).

B, Comparative profile of anatomic and fiducial RMSE values for each subject. Subject 2 has identical RMSE values for both the anatomic and fiducial registrations.

Clinical Applications

The results of the evaluation of the efficacy of the registered images for clinical use are shown in Table 2. The combined images provided significantly more conspicuous information than did conventional displays for two of the criteria considered: conspicuity of the relationship between the margin of the neural foramen and its contents, and conspicuity of the relationship between the margin of the spinal canal and its contents (a *P* value of less than .01 was considered significant). For the other criteria examined (conspicuity of the vertebral body, conspicuity of the posterior elements, conspicuity of the contents of the neural foramina, and conspicuity of the contents of the spinal canal), we found no statistical difference in clarity between conventional images and fused images. Figure 4 (axial images at two comparable levels), Figure 5 (close-up of the axial images at one comparable level), and Figure 6 (midsagittal view) show the differences between conventional and registered images. The relationship between the bony margins of the neural foramina and the spinal canal, as well as their soft tissue contents, is more conspicuous on the registered images. For these sequences, registration was done with external fiducial markers.

Discussion

We have described a technique for combining MR images and CT scans of the cervical spine and evaluated its usefulness in delineating relationships between bony and soft tissue structures. We found that the use of external fiducial markers yields a slightly more accurate registration than do anatomic landmarks, and estimated the accuracy of this technique to be routinely within 1 to 2 mm, provided that the image resolution is adequate enough to locate the fiducial markers and that the cervical spine is properly aligned. This registration accuracy is comparable to that achieved by Hill et al (1), who used CT/MR image registration for the planning of surgery and radiation therapy. Additionally, we found the registered images to be superior to conventional images for delineating the relationship between bony and soft tissue structures of the neural foramina and spinal canal.

Anatomic Features verses External Fiducial Markers

Image registration can be performed in a variety of ways, including use of a stereotaxic frame, external fiducial markers, and/or internal anatomic landmarks (7–9). Each of these methods has benefits and disadvantages. With external fiducial markers, the images must be acquired prospectively. For the higher resolution requirements of CT and MR image registration, technique-specific fiducial marker systems that fit onto stereotaxic frame-base rings have been used, but these can cause pain or discomfort for the patient (8). Anatomic landmark registration can be performed retrospectively; however, this method relies on accurate location and reproducibility of pointlike anatomic structures within the region of interest (9). In our study, we found that the accuracy of registration was greater with the use of external fiducial markers than with anatomic landmarks. There are two reasons why anatomic landmarks are less accurate in the context of the cervical spine. First, it is difficult to identify pointlike anatomic structures in this region on MR and CT studies. As described by Hill et al (1–3), examples of these anatomic points include 1) the junction of two linear structures, 2) the intersection of a linear structure with an approximately normal surface, 3) the intersection of three surfaces, 4) a minimum or maximum of 2D curvature of a linear structure, and 5) a minimum or maximum of 3D curvature of a surface structure. Although certain landmarks (eg, the transverse foramina) are easily identifiable at multiple levels on both CT and MR images, it is important to disperse the landmarks in a noncoplanar distribution to achieve maximum registration accuracy. It would not be appropriate, for example, to use the transverse foramina on multiple levels of the cervical spine as landmarks, because images may be slightly rotated around the central axis of the transverse foramina in relation to one another.

Second, the accuracy of registration increases with the number of landmarks identified and with the dispersion of the landmarks to the periphery of

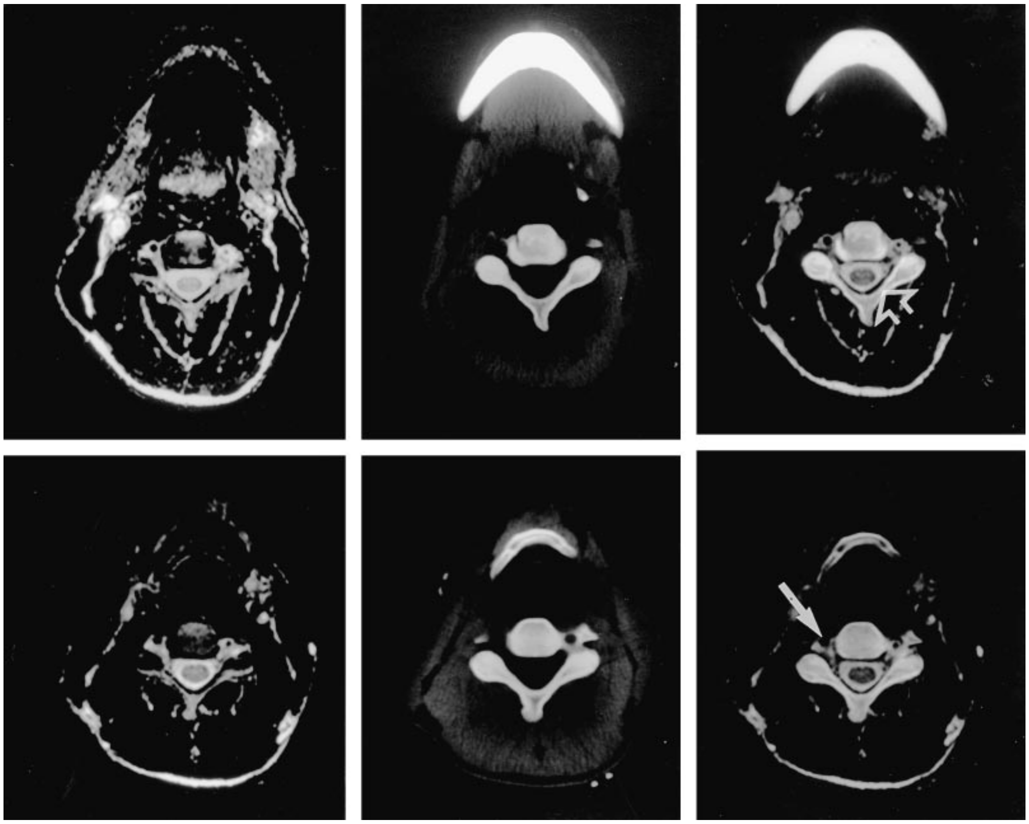

FIG 4. Multiple axial images from one subject (subject 2 from Fig 3B) include corresponding MR image (*left*), CT scan (*middle*), and registered image (*right*) of the cervical spine at the level of the neural foramina (two levels). This was the format used by the three neuroradiologists to compare the clarity of conventional images (MR and CT studies side by side) with that of the registered images. The relationships between the margins of the neural foramina (*solid arrow*) and spinal canal (*open arrow*) and their contents, respectively, are more conspicuously delineated on the fused image. The images were registered using external fiducial landmarks.

the data set. In this study, the number of anatomic and fiducial landmarks used was kept constant between the two registration methods. However, the spatial orientation differed between the anatomic and fiducial landmarks in that the anatomic landmarks were more centrally located and the fiducial markers were more dispersed to the periphery.

While statistically different, the difference between the RMSE values of the anatomic and fiducial registration methods was small, such that there were no obvious visual differences between the registrations. Indeed, in one subject, the RMSE values were identical. The major advantage of using anatomic features to register images is that registration may be done retrospectively, without manipulating the patient. The experience of the person selecting the landmarks (given an appropriate knowledge of anatomy), as well the reproducibility of locating them, are important considerations when using this method of registration (9). Also, increasing the number of anatomic landmarks may improve the accuracy of the registration. We suggest that further refinements in the localization and reproducibility of anatomic landmarks within the region of the cervical spine coupled with refined algorithms, which account for differences in alignment (see below), would allow for retrospective registration.

Alignment and Registration

Previous studies with forebrain images have validated the use of anatomic landmarks for retrospective registration (1–4). However, these studies did not encounter the technical difficulties in aligning the different examinations that we did. A limitation of our study was that the registration program we used did not incorporate significant differences in alignment of the CT and MR images of the cervical spine, as exemplified in one of our subjects. This limitation is a problem for both retrospective anatomic and fiducial registration. While simple warping algorithms may be able to approximate and correct misalignment due to cervical spine flexion or extension, a more detailed model incorporating vertebral dynamics with both rigid bodies and flexible segments would provide better registration that maintains anatomic integrity. In some clinical situations (eg, cervical trauma), the patient may have a neck brace on for both examinations, thereby indirectly controlling for differences in alignment and allowing for anatomic retrospective registration.

Clinical Application

The results suggest that our 3D image registration technique is most useful for evaluating the re-

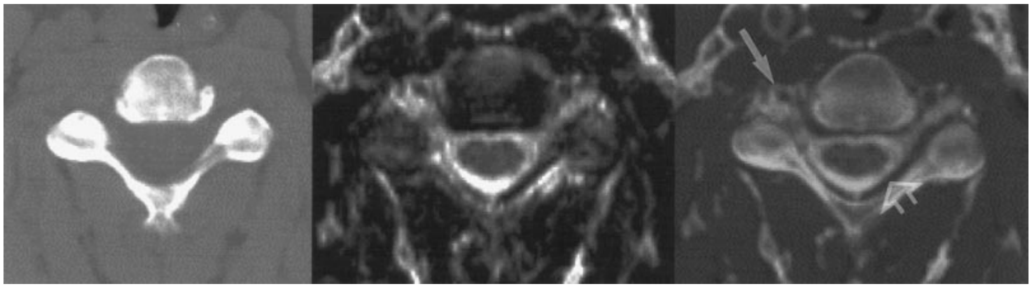

FIG 5. Magnified view of the axial images of the cervical spine at a comparable level (CT scan, *left*; MR image, *center*; registered image, *right*). The relationship between the margins of the neural foramina (*solid arrow*) and spinal canal (*open arrow*) and their contents is more conspicuously delineated on the registered image. The images were registered using external fiducial landmarks. Subject 5 from Figure 3B is represented.

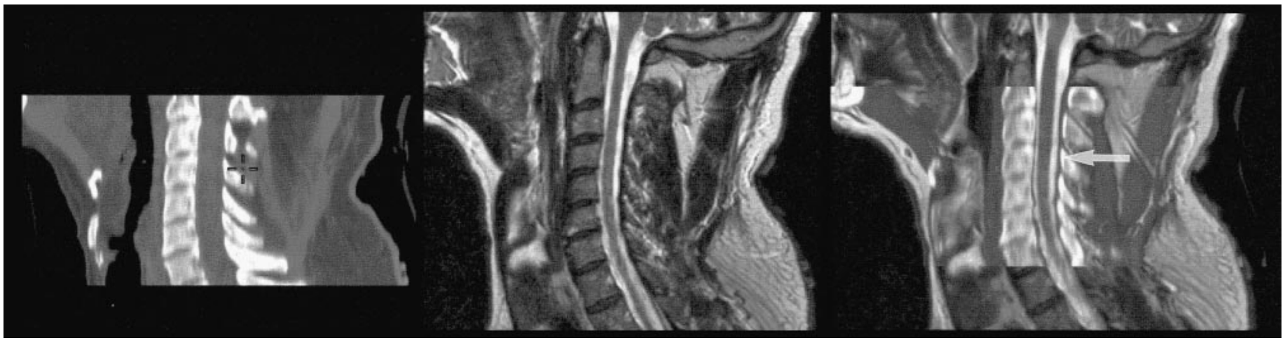

FIG 6. Corresponding midsagittal CT (*left*), MR (*middle*), and registered (*right*) images of the cervical spine show proper alignment and the relationship between the margin of the spinal canal (*solid arrow*) and its contents. The images were registered using external fiducial landmarks. Subject 4 from Figure 3B is represented.

lationship between bony and soft tissue structures. It is appropriate for use in patients with clinical neurologic problems that require accurate representation of the relationship between bony structures (normal and abnormal) and soft tissue structures (normal and abnormal). The clinical contexts in which this registration process may be most applicable are degenerative spondylosis and trauma. For evaluating cervical spondylosis, CT is clearly superior to MR imaging in identifying osteophytes, and it may be useful as an adjunct to MR imaging to help distinguish disk tissue from osteophytes (10–12). MR imaging may miss osteophytes adjoining a herniated nucleus pulposus, because the osteophytes may vary in signal intensity, probably reflecting differences in marrow content. Herniated disk material within the neural foramen may be difficult to identify on MR images. Asymmetric narrowing of neural foraminal fat on axial MR images may either indicate forminal stenosis due to a herniated nucleus pulposus or osteophyte or reflect partial-volume averaging of surrounding bone due to scoliosis or to a failure to center the scan through the neural foramina. By using this registration technique, it is possible that one may differentiate between osteophytes and herniated nucleus pulposus and better delineate the neural structures compromised. For trauma, the registration technique may enable one to directly observe the relationship between the bony and soft tissue injury. To definitively determine its clinical value, this registration technique will need to be applied in patients with cervical spondylosis or trauma.

Conclusion

We have described a technique that combines MR images and CT scans of the cervical spine. We found that the use of external fiducial markers yields slightly better registration than do anatomic landmarks, with an estimated accuracy routinely within 1 to 2 mm. The accuracy depends on similar neck alignment for both examinations. Additionally, we found that, in healthy subjects, registered images are superior to conventional images for delineating the relationship between bony and soft tissue structures of the neural foramina and spinal canal.

Acknowledgments

We thank Philip F. Morway, Micheal D. Proctor, and Micheal J. McVeigh for technical assistance.

References

1. Hill DLG, Hawkes DJ, Gleeson MJ, et al. **Accurate frameless registration of MR and CT images of the head: applications in surgery and radiotherapy planning.** *Radiology* 1994;191:447–454
2. Hill DLG, Hawkes DJ, Crossmann JE, et al. **Registration of MR and CT images for skull base surgery using point-like anatomical features.** *Br J Radiol* 1991;64:1030–1035

3. Hill DLG, Hawkes DJ, Hussain Z, et al. **Accurate combination of CT and MR data of the head: validation and applications in surgical and therapy planning.** *Comput Med Imaging* 1993; 17:357–362
4. Gandhe AJ, Hill DLG, Studholm C, et al. **Combined and three-dimensional rendered multimodal data for planning cranial base surgery: a prospective evaluation.** *Neurosurgery* 1994;35: 463–471
5. Arun KS, Huang TS, Blostein SD. **Least square fitting of two 3D point sets.** *IEEE Trans Pattern Anal Mach Intell* 1987;9:698–700
6. Zar JH. ***Biostatistical Analysis.*** 2nd ed. Englewood Cliffs, NJ: Prentice Hall; 1984:386–387
7. Pelizzari CA, Chen GTY, Spelbring DR, Wrichselbaum RR, Chen CT. **Accurate three dimensional registration of CT, PET and/ or MRI images of the brain.** *J Comput Assist Tomogr* 1989;13: 20–26
8. Henri CJ, Collins DL, Peters TM. **Multimodality image integration for stereotaxic surgical planning.** *Med Phys* 1991;18:167–177
9. Strasters KC, Little JA, Buurman J, Hill DLG, Hawkes DJ. **Anatomic landmark image registration: validation and comparison.** *CVR Med/MRCAS* 1997;3:79–22
10. Russell EJ. **Cervical disk disease.** *Radiology* 1990;177:313–325
11. Tsuruda JS, Norman D, Dillon W, Newton TH, Mills DG. **Three-dimensional gradient-recalled MR imaging as a screening tool for the diagnosis of cervical radiculopathy.** *AJNR Am J Neuroradiol* 1990;10:1263–1271
12. Georgy BA, Hesselink JR. **MR imaging of the spine: recent advances in pulse sequences and special techniques.** *AJR Am J Roentgenol* 1994;162:923–934