Registration of 3D cerebral vessels with 2D digital angiograms: Clinical evaluation

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Running head: Registration evaluation

ABSTRACT

Rationale and Objectives: This report evaluates the accuracy and speed of a new, semi-automatic method of 3D-2D vascular registration. We intend to use this registration method to help guide endovascular procedures by interpreting each DSA image in terms of pre-created 3D vessel trees that contain parent-child connectivity information.

Materials and Methods: Three-dimensional, connected vessel trees are created from segmented MRA data. We report registration of such trees with 11 DSA images, using both our method and the "gold standard" of manual registration. We compare the accuracy of each registration method using Repeated Measures ANOVA with correction for heterogeneity of variance to evaluate separation of curve pairs on the viewplane. Subjective clinical comparisons of the two registration methods are evaluated by sign test. Registration time is evaluated for both methods and as a function of the error in initial estimate of MRA position.

Results: Our registration method produces results numerically superior to those of the "gold standard" of manual registration ($p<.001$), and was subjectively judged as good or better by clinical reviewers. Registration time by our method was faster ($p < .001$). If the rotational error in the initial estimate of MRA position is less than 10^{o} around each axis, registration takes 1-2 minutes.

Conclusion: The proposed method produces results as good or better than those of manual registration. It is also fast enough to be used to calculate an initial registration matrix during endovascular embolization and for intermittently adjusting registration updates provided by automatic tracking systems.

Indexing terms: Registration, MRA, DSA, angiography, blood vessels, intracerebral vessels

Key words: Registration, DSA, MRA, angiography, interventional radiology

INTRODUCTION

The rapid rise of intracerebral endovascular procedures has emphasized the need for better ways to interpret digital subtraction angiograms (DSAs) in three dimensions (3D). There have been many approaches to the problem, most notably several commercial companies' ongoing effort to reconstruct sequences of DSA images into 3D. Even if such approaches reach the level of clinical utility, however, they still will not provide optimum information as they do not describe the vasculature in terms of a 3D, connected tree.

If the clinician could interpret each DSA image in terms of a connected, 3D vascular tree, endovascular procedures would be both easier and faster. 3D connectivity information allows estimation of collateral flow to an area, simulation of catheter passage through a 3D vessel tree, and quick definition of vascular branches supplying a tumor. This kind of information, containing not only the 3D locations of vessels but also their parent-child relationships, is difficult to obtain from simply looking at sequences of grayscale images. No current imaging method provides this kind of information.

We hope to provide this kind of aid to interventionalists. The approach is to extract vessels from magnetic resonance angiograms (MRA), and to organize them into 3D trees containing connectivity information[1, 2, 3]. Use of these vessel trees during embolization procedures should allow rapid evaluation of catheter trajectories with less catheter manipulation and with fewer DSA views than is now possible.

In order for the interventionalist to interpret this kind of 3D data, 3D vessel trees must be registered with each intraoperative DSA image. The purpose of this report is to evaluate a new method of 3D-2D vascular registration[4]. If successful, the approach would allow interpretation of each DSA image in terms of 3D vessel trees in a fashion heretofore impossible.

This report analyzes the both the accuracy and the speed of our registration method. Under conditions of image distortion, perfect registration is impossible. We therefore evaluate both the absolute error produced by our method and compare the error to that produced by the "gold standard" of manual registration. We also evaluate the time required. We conclude that our method produces results as at least as accurate as those of manual registration. Unlike manual methods, it is also fast enough to be used to calculate an initial registration matrix and to intermittently adjust registration updates provided by fast, automatic tracking systems.

METHODS

1. Definitions and overview

The term "vessel" refers to a 3D vascular segment. The term "3D curve" refers to the skeleton of a vessel defined from an MRA. A "2D curve" represents either the projection of a 3D or the skeleton of a vessel projection defined on DSA. A "vessel tree" is a set of vessels extracted from an MRA and linked to represent a connected portion of the circulation. The word "pose" refers to the position and orientation of the MRA within the coordinate system of the DSA unit.

This report provides four analyses of our registration method. The first 3 analyses compare the results of our method to those of manual registration. The 4 analyses include 1) objective valuation of accuracy using the distance from points on the DSA to the nearest point on a vessel projection, 2) subjective valuation of accuracy by external reviewers, 3) registration time, and 4) time required by our method as a function of error in the initial estimate of MRA pose.

Each analysis uses data obtained from 2 patients and includes 11 DSA views of 3 carotid circulations. All tests were conducted on a 233 MHz Pentium machine running Windows 95.

Image acquisition and image distortion corrections

Three-dimensional, time of flight MRA was performed in a 1.5T MR scanner (Vision, Siemens Medical Systems, Iselin, NJ) with a quadrature head coil. Off resonance (1500 Hz) magnetization transfer suppression (75 Hz) was used to further suppress background stationary tissue. Axial images were obtained over a 6.4 cm (patient 1) and 8.5 cm (patient 2) volume using contiguous sections. Voxel size was 0.86 * 0.86 * 1.1 mm in both studies.

DSA images were acquired from two units. The first, a mobile C-arm unit (#9600, OEC, Salt Lake City, Utah), produced images of 459 x 484 pixels. The second, a permanent uniplane unit (Multistar, Siemens Medical Systems, Iselin, NJ), produced images of 1024 x 1024 pixels. Each patient was imaged by a different angiographic unit. The field of view ranged from 8 - 21^{o}.

Both DSA and MRA images contain distortions likely to interfere with 3D-2D registration. 2D distortion errors and MR machine-specific distortions were corrected by imaging appropriate phantoms. However, we have not corrected MR patient-specific errors, such as the distortions present in areas close to a tissue-air interface.

2. Extraction of vessels from MRA data and creation of vascular trees

Extraction of a vessel involves 3 steps: definition of a seed point, automatic extraction of an image intensity ridge representing the vessel's skeleton, and automatic determination of width at each skeleton point[1]. Automatic tree creation can then be performed beginning from interactively selected roots[2, 3].

3. Registration of a 3D vascular tree with a 2D DSA image

For the purposes of this paper, registration of a 3D vascular tree with a 2D DSA image is defined as determination of the pose (position and orientation) of the 3D tree within the coordinate system of the DSA imaging device. One means of registration uses mouse movements to manually rotate and translate the 3D dataset until the projections of its 3D curves superimpose the curves seen by DSA ("manual registration"). When performed by an experienced operator with unlimited time, the quality of registration is usually excellent. We view this method as the "gold standard".

Liu developed the registration method evaluated in this report[4]. The approach uses vessels and their projections as internal fiducial markers. The primitives are 4 - 8 2D curves extracted from the DSA and an equivalent number of 3D curves extracted from the MRA. The program then optimizes a viewplane based disparity measure based on the iterative closest point paradigm between the DSA skeletons and the projections of the MRA skeletons. Newton's method on the pose parameters in 3D is used to iteratively refine the solution.

This method requires manual definition of 4 – 10 curves on the DSA and association of each such curve with the projection of a 3D curve. If the initial projection of the MRA differs greatly from that of the DSA, the user must manually translate and rotate the 3D tree into a better starting position so as to be able to associate curve pairs. For the time analyses in this report, "registration time" represents the total user time required, including the time for curve definition and any initial, manual adjustment of pose.

4. Evaluation protocols

a) Accuracy evaluation: Euclidean distance between curve points on the viewplane

Two registrations, one manual and one by our method, were performed for each of the 11 DSA images. Each registration pair used the same set of 3D curves, the same DSA image, and the same initial estimate of MRA pose. The two registrations were performed in random order. The initial estimate of pose was that defined by an AP or lateral DSA view of a third patient. Rotational differences between the input pose estimate and final calculated pose ranged from about 15 degrees to about 60 degrees.

A physician experienced in both registration methods performed all registrations. Once a pair of registrations was completed, the user returned to the image of the first registration and, for each 3D curve projection, manually defined the 2D DSA curve that corresponded most closely. The program automatically interpolated each set of curve points. For each pixel along each DSA curve, the program then calculated the distance in mm to the closest point along the projection of the associated 3D curve. These calculations were repeated for the second registration, using the same set of 2D DSA curves. Paired distance calculations were thus done for each point along each DSA curve, one for manual registration and one for our registration method.

Statistical analysis of the data addressed the null hypothesis “Do the two registration methods produce identical performance?” and used average distance across vessels as the outcome measure. For each DSA curve, the average distance between its points and the associated 3D curve projection was first computed for each registration method. In order to account for the correlation of repeating registration on the same image, a Repeated Measures ANOVA was then used, with registration type as a within-subject factor and patient a between-subject factor. The differing number of points on each 2D curve introduced heterogeneity of variance, which was approximately adjusted for by applying a transformation matrix. Two other sources of correlation, observation of multiple points on the same curve and of multiple vessels on the same image, were not analyzed because inclusion of these factors would complicate the analysis, leading to an unstable statistical model. Hypothesis tests were conducted to test the main effects of registration method and patient, as well as an interaction between the two.

b) Accuracy evaluation: subjective assessment

As a subjective measure of registration quality, two neuroradiologists compared the 11 pairs of registrations described above. Each radiologist viewed a program in which associated pairs of registrations were shown side by side. Each radiologist filled out a form in which the two registrations were evaluated by a 7 point scale (left much better, left better, left possibly better, the two are equal, right possibly better, right better, and right much better). The registration displayed at left was randomly determined.

Statistical analysis addressed the null hypothesis: “Do external reviewers subjectively feel that the performance of the two registration methods is identical?”. For analysis, the seven point scale was reduced to a 3 point scale. For each reviewer separately, the subjective evaluation was tested using a sign test[5].

c) Registration time: comparison of methods

The 22 registrations described above were each timed to the nearest minute. Registration time by our method was considered to be the total time required, including curve definition and association, any preliminary manual registration employed, and the program’s time for automatic registration. Statistical analysis addressed the null hypothesis: “Is the time required for each registration method the same?” The differences in time between the two methods were compared using a sign test[5].

d) Registration time: dependence upon initial starting position

The results of study c) above indicated variability in the time required for registration. For registration by our method, the most time-consuming cases were those in which the initial estimate of MRA pose was greatly different from that shown by the DSA, requiring an initial, manual adjustment before curve pairs could be associated. It therefore seemed useful to examine registration time as a function of the error in initial pose estimate.

One additional registration was therefore performed for each DSA view. In each case the starting registration matrix was that obtained following registration in study a) above, but the matrix was modified to include a rotation in x, y, and z of n degrees and a translation in x, y, and z of n/5 mm, with n = 2, 4, 6, 8, 10, 15, 20, 25, 30, 40, or 50. Rotations were performed around the center of the MRA. Each value of n was used once and each DSA was registered once, but DSA-n asignations were random. The sign of n was determined randomly for each rotation and translation. If an initial, manual adjustment was required, this was recorded. We did not time multiple registrations of the same DSA because of the effect of learning upon registration speed.

RESULTS

Figures 1 and 2 illustrate a registration by our method for each of the two patients in this study. Each figure shows the initial projection of the vessels against the DSA, the DSA curves used for registration, and the results after registration. Both vessel trees failed to include the distal vasculature because the MRA did not include the entire head. Within the defined MRA volume, however, each vessel tree is detailed and matches the DSA. As indicated by arrows, minor registration errors often occurred at the periphery and skull base, where tissue-air interfaces are present and MR vessels are likely to exhibit distortion.

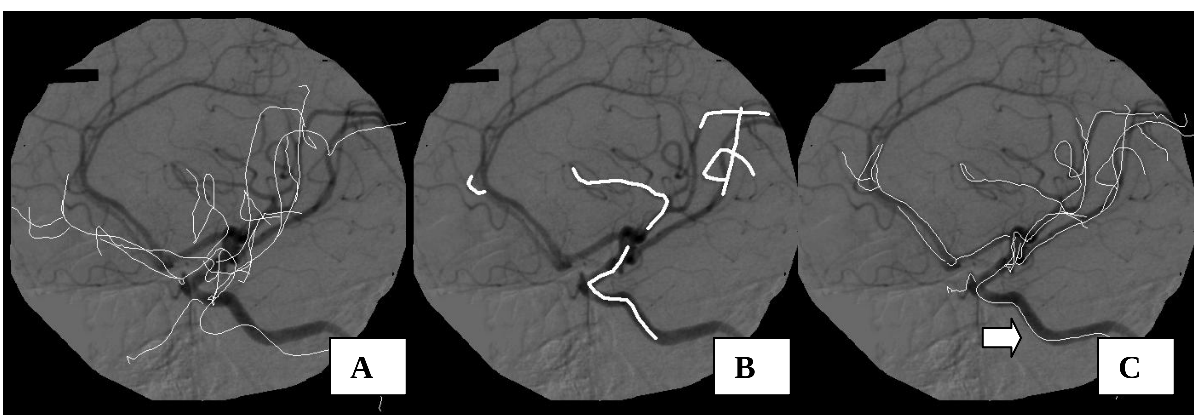

Figure 1: Results of registration. A. Vessel skeletons are projected in grey upon DSA. The initial pose estimate is about 15 degrees away from the pose determined by registration. **B.** The 6 2D curves used for registration are shown in white. **C.** Results of registration. The arrow points to a slight misregistration of the carotid where it courses adjacent to the air-filled sphenoid sinus.

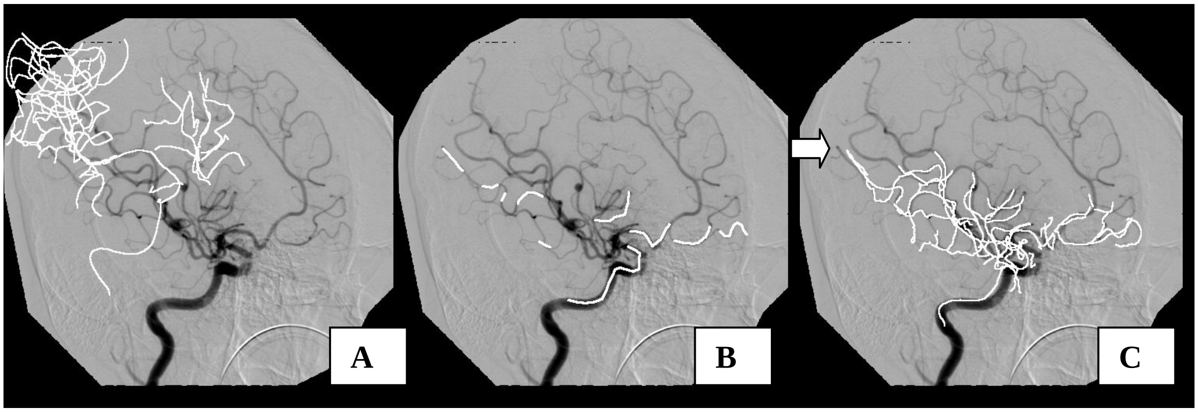

Figure 2: Results of registration. The patient is different from that shown in Figure 1. **A.** Vessel skeletons are projected in white upon a DSA image. The initial estimate of pose is inaccurate by about 60 degrees with additional translational error. **B.** The 10 2D curves defined and used for registration are shown in white. **C.** Results of registration. The arrow points to a slight misregistration of a distal vessel.

Accuracy evaluation: Point separation on the viewplane

A total of 48,081 DSA curve points were defined on the 11 DSA images. For two curves, the initial output file indicated a mean distance of close to 2 cm between the points on the DSA curve and the projection of the associated 3D curve by both registration methods. Inspection of the registered images did not reveal this kind of egregious error. The most likely explanation is user error in curve association. To examine the impact of these two questionable associations on the validity of the results, analysis was performed both with and without the two curves. The results and conclusions were not affected. Table 1 shows the means and standard deviations of the distances between each DSA point and the closest point along the associated 3D curve projection. These results represent the 47,775 points analyzed when the two questionable curves were omitted from study. Lower mean values indicate a better registration.

Formal statistical analysis noted a significant difference in results by registration type ($p < 0.001$), indicating that average distances between point pairs were lower using our registration method. The patient shown in Figure 1 had significantly higher average point separations by both registration methods than did the patient shown in Figure 2. This result is not surprising, as the first patient's DSAs were obtained using a portable machine that produced images with relatively large pixels and large distortion errors. Statistical analysis showed no registration method by patient interaction (p = 0.37), indicating that the reduction in registration error attributable to using our method was of the same magnitude in both patients.

	OUR REGISTRATION	MANUAL REGISTRATION	# POINTS
PATIENT 1	0.7 ± 0.6 mm	0.8 ± 0.7 mm	11,977
PATIENT 2	0.3 ± 0.4 mm	0.5 ± 0.5 mm	35,798

Table 1: Mean point separations by patient and registration type. The first two columns represent the means and standard deviations of the distance in mm between DSA curve points and the closest projection point of the associated 3D curve. The third column gives the number of points analyzed for that patient.

These results indicate that both methods are capable of producing good registration. By both methods, the mean distance between DSA points and the closest point on the projection of the associated 3D curve is less than a mm. Our method appears to produce numerically superior results, however. This improvement in accuracy also appears to be maintained when applied to DSA images of varying quality.

b) Accuracy evaluation: subjective assessment

The two neuroradiologists' subjective evaluations of registration pairs showed a slight but statistically insignificant preference for our registration method (p = 0.12 for reviewer 1 and p = 0.15 for reviewer 2). Figure 3 illustrates the results using the original 7 point scale. The data here are organized so that a value of 1 indicates our registration method to be much better, a value of 7 indicates manual registration to be much better, and a value of 4 indicates the two methods to be equivalent. These results suggest that, by subjective valuation, our method produces registrations at least as good as those of manual registration.

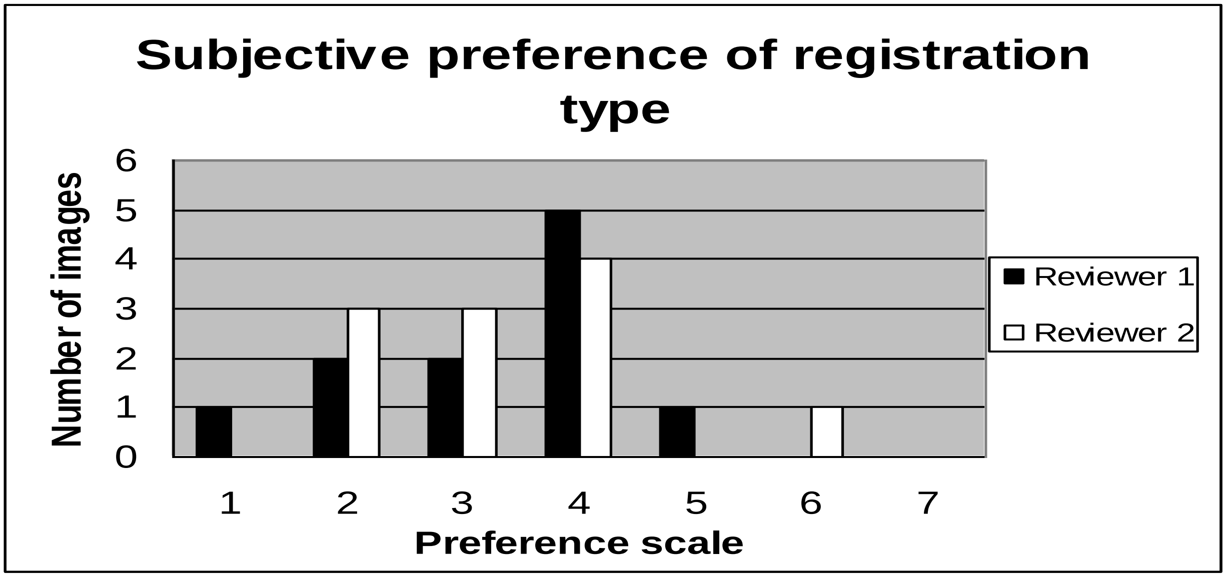

Figure 3: Subjective evaluation by external reviewers of 11 registration pairs. The X axis represents viewer preference (1 = ours much better, 2 = ours better, 3 = ours may be better, 4 = the two methods are equivalent, 5 = manual may be better, 6 = manual better, 7 = manual much better). The Y axis indicates the number of images assigned by each reviewer to each category.

c) **Registration time: comparison of methods**

For the 11 pairs of registrations performed, registration by our method was always performed more quickly than was manual registration. To the nearest minute, the mean time to completion by our method was 9 ± 4 and by the manual method 32 ± 13 minutes. Statistical analysis indicated the difference to be significant ($p < 0.001$).

For our registration method, the automatic registration itself takes approximately 30 seconds. Defining and associating curves takes about one minute. However, when the initial estimate of MRA pose was very inaccurate, 2-20 minutes could be spent in manual manipulation of the MRA projection so as to find a pose from which the user could associate curve pairs.

d) Registration time: dependence upon initial starting position

The results above suggest that our registration method is subjectively at least as good and is numerically more accurate than the manual registration method. Our method can also be performed more quickly than can manual registration. However, a mean registration time of 9 minutes is too slow for our intended use. As outlined under **Methods**, we therefore performed a time test of our registration method as a function of the amount of error present in the initial estimate of the pose of the vessel tree.

Figure 4 illustrates the results of this time test. The value of “n” indicates the amount of error in the intial estimate of MRA pose, as described under **Methods**. Stars appear above registrations in which a preliminary manual registration was required before our algorithm could be applied. As with the previous time test, the time for registration indicates the total time required, including any time needed for preliminary manual registration and curve definition.

As shown by this graph, registration can be done in 1-2 minutes if the initial estimate of the MRA pose has less than a 10 degree rotational error around each major axis. For larger errors in the initial pose estimate, a preliminary manual registration is usually required and the total registration time becomes both more variable and much longer.

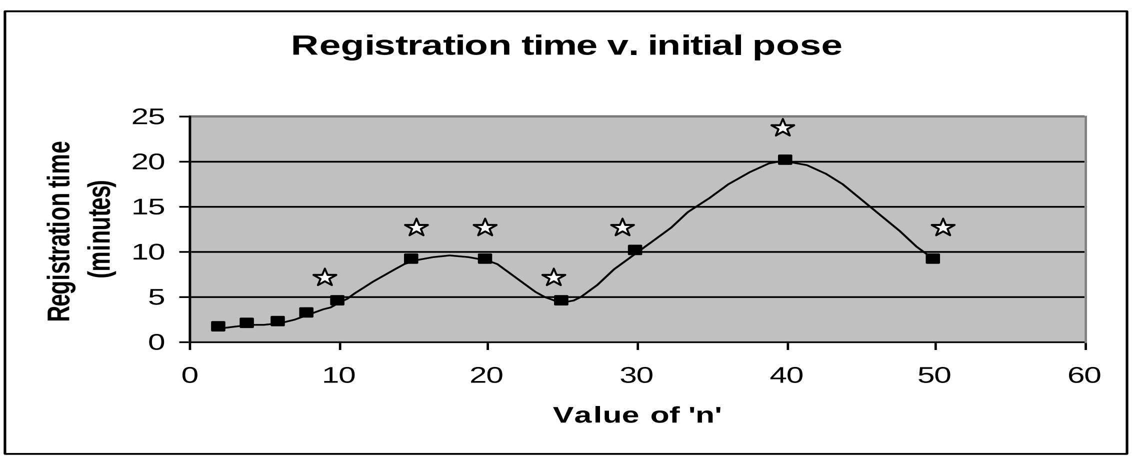

Figure 4: Registration time v. error in initial pose estimate. The definition of ‘n’ is given under Methods. Stars indicate registrations in which a preliminary manual registration was required. Registration time refers to the total registration time, including any preliminary manual registration required.

DISCUSSION

Our long-term goal is to provide better ways of displaying 3D vascular anatomy for guidance of surgical and endovascular procedures. Most approaches to the problem have emphasized simple visualization of greyscale images. By contrast, our approach also stresses the importance of providing a direct, symbolic description of vessel connectivity. For the interventional radiologist, the most obvious advantage of this approach is the ability to simulate catheter passage through a 3D vascular tree. One may thus select optimal catheter pathways with minimal exploration. No currently available imaging system gives the interventionalist this kind of information.

Our approach precreates 3D vascular trees. In order for these trees to be used during endovascular procedures, they must be rapidly and accurately registered with DSA images. One means of registration is by stereotactic frame. However, stereotactic frames are invasive and are not compatible with a full range of angiographic views. A second method involves external fiducial markers. However, markers on the skin may move, tend to be localized to a particular region thus providing only locally accurate registration, and, like the stereotactic frame, become useless from some angles of view and under some magnifications.

The registration method we employ uses vessels and their projections as internal fiducial markers. The approach is non-invasive, does not require placement of external fiducials, and applies to DSAs obtained from any angle and at any magnification. This report evaluates both the accuracy and the time requirements of this registration method using data obtained from two different patients, two different angiographic units, and 11 DSA images representing a range of views and magnifications. If, by these tests, the method appears both accurate and fast enough for clinical use, we can begin to employ it in the endovascular suite.

1. Registration accuracy

Previous work has evaluated our 3D-2D registration method using phantom DSAs, created from synthetic projections of vessel trees[4]. Under these test conditions the true pose of the vessel tree was known and image errors were absent. In tests that compared the true and calculated positions of each 3D point after registration, the largest misregistration of the thousands of 3D points analyzed was consistently less than a millimeter[4]. Under idealized conditions, the method is therefore capable of extraordinary accuracy.

Equal accuracy is impossible under the clinical conditions of MRA-DSA registration. In particular, image distortions may deform the curves used for registration. Although we correct for distortions in both the 3- and 2D image data, some errors remain. Both Chapman[6] and Michiels[7] report significant distortions in MR data close to a tissue-air interface. We have not yet encountered difficulties of the magnitude suggested by either group. However, our clinical registrations have consistently shown slight but noticeable errors, as described and shown by this report.

As the true pose of the MRA relative to the DSA is unknown, we cannot easily assess accuracy by comparing the true and calculated positions of 3D points. This report therefore analyzes both point separation on the viewplane and subjective evaluation of results by external experts. Both the objective and subjective evaluations include comparison with the "gold standard" of manual registration. These two studies suggest that the results of registration by our method are subjectively at least as good and are numerically superior to results obtained by manual registration. Our numerical results are also as good or better than those reported by other groups describing 3D-2D vascular registration methods[6, 8]. We additionally include subjective evaluations of registration accuracy as judged by clinical experts.

2. Registration time

3D-2D registration must be performed rapidly if it is to be of use during endovascular procedures. Several groups have described registration of segmented MRA data with DSA images but do not give the registration time required [6, 8]. Feldmar uses 2 DSA views simultaneously and reports 3 minutes for each registration[9]; it is not clear whether this estimate also includes the time needed for DSA segmentation. Kita presents a fully automated registration metric that operates in seconds[10]. However, the 3D segmentation method appears to extract only a few vessels, of which only 3 appear to be used both for registration and evaluation. The registrations shown also do not involve either heavy projection overlap or major rotational errors in the initial estimate of MRA pose. It is therefore unclear that the algorithm will perform successfully if many vessels are available, when the registration involves complex conditions such as those shown in Figure 2, or when more than highly local registration is desired.

The registration algorithm analyzed in the current paper can handle conditions of extensive projection overlap and produces good results even with large errors in the initial estimate of MRA pose. Registration is performed in 1 – 2 minutes under conditions in which rotational errors in the estimate of MRA pose are less than 10 degrees around each axis. More time is required to provide a good registration that begins from a grossly erroneous estimate of MRA pose. These time requirements are too large for the registration algorithm to be used in isolation under clinical conditions in which frequent, large changes are made in the fluoroscopic imaging position. However, the approach seems suitable for providing an initial registration and for intermittently making small corrections in subsequent registrations guided largely by fast, commercially available tracking systems. We will use this approach to provide the interventionalist useful information that is unavailable by any current imaging method.

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