Angiographic Film Subtraction Using a Laser Digitizer and Computer Processing

John M. Boone, Neva M. Corrigan, Stephen T. Hecht, and Daniel P. Link

Digital subtraction angiography has been accepted as an invaluable clinical tool over the past decade; however, film-screen-based angiography is still performed routinely when high-resolution or large field-of-view angiograms are needed. A technique is presented whereby two films from an angiographic sequence are digitized using a high-resolution laser digitizer, and the digitized images are aligned, subtracted, and displayed using the computer. To accommodate for some types of patient motion, an image warping algorithm is presented and discussed in detail. The warping algorithm is piecewise linear, using triangular regions for warping, resulting in a global nonlinear transform across triangle elements. An algorithm describing optimal triangle selection also is discussed. The results show that subtraction images of excellent quality can be produced by the proposed technique, and suggest that, in some settings, digitized subtraction films may be preferred over conventional film subtraction.

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KEY WORDS: angiography, film subtraction, warping algorithm, digital image processing, image registration.

FILM SUBTRACTION is typically used in angiography when the spatial resolution requirements of the clinical examination exceed the capabilities of digital subtraction angiography (DSA). In neuroangiography, for example, the identification of smaller vessels can be clinically germane, because slight flow perturbations can have substantial physiological consequences. Detection of minute neural irregularities can be of great clinical significance, as in the evaluation of vasculitis. Tiny vessels and subtle wall irregularities cannot always be depicted using $1,024 \times 1,024$ DSA with typical image intensifier fields of view. In peripheral vascular angiography, high spatial resolution arteriography is required to assess subtle changes in the vascular wall, which determine the suitability of the vessel for grafting.

In film subtraction, two radiographic films from

an angiographic sequence are selected; the *mask* is the film angiogram acquired just before contrast media has arrived in the vasculature of interest and therefore is basically an image of background anatomy; the *contrast image* is the film angiogram acquired during the maximum opacification of the vessels of interest; this image shows the contrast-agent-filled vessels overlying the background anatomy.

The first step in producing a film subtraction is to produce a *subtraction mask* from the mask image. This is done using a radiographic copying system (a light box with a timer in a darkroom) and special subtraction mask film that is negative (standard film for copying radiographs is positive film) with an average gradient near 1.0 (standard radiographic film has an average gradient of near 3.0). The subtraction mask is, in theory, exactly the same as the mask except that it is inverted in optical density; for instance, the original mask film shows white vessels on a black background, whereas the subtraction mask film shows black vessels on a white background. The subtraction mask is overlaid onto the contrast image, such that the regions in the superimposed image that have not changed between scenes (the static patient anatomy) become

From the Department of Radiology, University of California, UC Davis Medical Center, Sacramento, CA.

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Address reprint requests to John M. Boone, PhD, Department of Radiology, FOLB 2E, 2421 45th St, Sacramento, CA 95817.

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Fig 1. The triangles used for each warping element are illustrated. The six pairs of coordinate values are used to calculate warping parameters, which are used to transform (pixel by pixel) the contents of the primed coordinate triangle into the unprimed coordinate triangle.

uniformly gray (in theory), while the contrast-filled vessels appear white. By inverting the contrast image rather than the mask image, contrast-filled vessels can be made to appear black on the subtracted image.

Photographic subtraction is essentially optical cancellation through the addition of inverse im-

ages, but the two overlaid films typically result in a very dark image when viewed on standard light-boxes. Therefore, the final step in the film subtraction process is to make a copy film of the superimposed images, adjusting the copy exposure time to produce a single subtraction film with optical densities (OD) in the clinically useful range (approximately 0.5 to 2.5).

Film subtraction under ideal conditions results in the removal of the patient's static background anatomy, which is not of interest in angiography; therefore, a significant source of structured noise is eliminated from the film. This improves the effective signal-to-noise ratio and the diagnostic image quality. Although a properly obtained film subtraction of an angiographic sequence in which there is no patient motion can produce beautiful images, practical realities such as patient motion (between the acquisition of the mask and the iodinated image) and the nonlinear characteristics of the screen-film detector system often compromise the quality of the images. In addition, the material and personnel expenses of producing the two additional films required for film subtraction are not insignificant.

Fig 2. Diagram shows the geometry (and defines the nomenclature discussed in the text) for the bilinear interpolation routine used. The point $P(x', y')$ is the point calculated on the primed coordinate image as a result of the warping procedure. The gray-scale value is interpolated for this point using bilinear interpolation as described in the text, and that value is then placed in the unprimed coordinate image.

Fig 3. Solid circles demonstrate the theoretical number of possible triangles that can be defined by the number of points indicated on the abscissa, which is equal to $N(N-1)(N-2)$. Using the criterion that triangles with points that fall within them are unacceptable ("after-point criterion," solid squares with 95% confidence limits), the number of usable triangles is reduced by more than an order of magnitude. The lower curve was calculated using random generated points on a surface, with 20 samples calculated at each point along the abscissa. The error bars show $\pm 2\sigma$.

Herein we report on a process in which the conventional film subtraction technique as described above is replaced by simply digitizing the mask and the iodinated image films using a high-resolution laser digitizer. All subsequent image handling is performed using computer software, with display options of both laser film or soft copy viewing on a high-resolution monitor.

MATERIALS AND METHODS

Materials

Angiographic film sequences were acquired from the neuroradiology and peripheral vascular services in our institution. The screen-film system (Fuji Medical Products, Tokyo, Japan) used was a 400-speed, 35-cm $\times$ 35-cm (14" $\times$ 14") system. The films were digitized to 12 bits using a high-resolution (50- μ m $\times$ 50- μ m pixel capability) laser digitizer (Lumisys 150, Sunnyvale, CA). The images used in this study were digitized to 100- μ m $\times$ 100- μ m pixels, resulting in five line pairs per millimeter of limiting resolution. Images were processed and analyzed using software written in our laboratory on a 166-MHz Pentium-based (Intel Corp, Sunnyvale, CA) personal computer with 64 megabytes of RAM, 9 gigabytes of disk storage, and a separate high-resolution (1,280 $\times$ 1,024) display system (DOME Imaging, Waltham, MA).

Image Processing

Image alignment. The digitized mask and contrast images are subtracted in the computer, and the difference image is displayed on the monitor. In general, a fair amount of translational misregistration is evident when efforts to register the

images are not taken. Because the films are aligned with a metal edge when inserting them into the film digitizer, there is very little gross rotational misregistration.

After digitization, the first processing first step is to crudely register the two images, using simple horizontal and vertical translation software coupled with the feedback of viewing the subtracted image. This step requires just a few inputs (using mouse- and cursor-driven software) and takes only a few seconds. Once the subtraction image is crudely registered and displayed on the monitor, a series of fiducial points is selected by the user. These fiducial marks are used to find matching points between the two unsubtracted images, using correlation. This process involves placement of a mouse-driven box (30 pixels by 30 pixels) in numerous locations around the image. The slight misregistration of the subtraction image helps in the positioning of the box-cursor; areas of high-frequency misregistration (sharp edges) are specifically sought, and these regions on the image show up well on the slightly misregistered subtraction image. The number of box-cursors placed on the image depends on the complexity of the subtraction image and the size and shape of the region where contrast filled vessels are

Fig 4. This figure shows six different triangles with different levels of skewness. An equilateral triangle has a skew parameter (S) of 0, and S increases as the amount of skew increases. $S = (\text{perimeter}^2/\text{area}) - S_{\text{equilateral}}$. Triangles with essentially colinear points can have very large skew parameters.

present. It is only necessary to align and subtract the two original images in areas where contrast-filled vasculature is to be enhanced through subtraction.

Once the N_{points} boxes have been placed, each box is evaluated using a simple least-squares minimization routine between the two unabstracted images. A series of shift values (δx , δy) are iterated over, searching for a minimum in the value

$$\chi(\delta x, \delta y) = \sum_{\delta x=(-A/2)}^{(A/2)} \sum_{\delta y=(-A/2)}^{(A/2)} \sum_{x''=(x'-B/2)}^{(x'+B/2)} \sum_{y''=(y'-B/2)}^{(y'+B/2)} [I_{\text{contrast}}(x + \delta x, y + \delta y) - I_{\text{mask}}(x, y)]^2 \quad (1)$$

Here, $I_{\text{contrast}}(x, y)$ is the iodinated image and $I_{\text{mask}}(x, y)$ is the mask image. A square region of $B \times B$ pixels centered at (x'', y'') is subtracted, the sum of the squares is computed, and a surface $\chi(\delta x, \delta y)$ of $A \times A$ pixels is evaluated for a minimum. The $(\delta x, \delta y)$ shift values corresponding to where $\chi(\delta x, \delta y)$ is at a minimum are selected, such that a fiducial mark on the I_{contrast} image at location $(x + \delta x, y + \delta y)$ corresponds to a location (x, y) on the I_{mask} image. This procedure is executed for all

N_{points} selected by the user, creating a series of matching points between the two unabstracted image. The values of δx and δy generally are different for each N_{points} on the image. If δx and δy were identical for all N_{points} on the image, this would correspond to simple linear transformation in each dimension.

Image warping. The warping procedure has been described elsewhere¹; however, because substantial improvement and embellishment to the algorithm has occurred, a complete description of the methodology is provided here. The alignment step described above results in a set of pairs of coordinates, where $I_{\text{contrast}}(x + \delta x, y + \delta y)$ corresponds to $I_{\text{mask}}(x, y)$. To simplify notation, let the alignment point pairs between the two images be represented as $(x, y) \leftrightarrow (x', y')$, where $x' = x + \delta x$ and $y' = y + \delta y$, and the unprimed coordinates (x, y) are on the mask image and the primed coordinates (x', y') on the contrast image.

The warping algorithm is based on a piecewise bilinear coordinate transformation. When the N_{points} coordinate pairs are selected in reasonable quantity (which depends on the amount of motion present between the two images), the piecewise bilinear warping algorithm results in a nonlinear spatial transform

Fig 5. An example of the hand placement of points used to define the triangle network for warping. Each point is hand placed, and the corresponding locations on both images to be subtracted are identified using image correlation/least squares comparison between the two images. The dotted line shows the outermost bounds of the warping algorithm, since only interpolation (not extrapolation) is used. Generally the points are located near sharp boundaries and edges, away from contrast-filled vessels.

Fig 6. The array of points illustrated in Fig 5 is shown here four times, each with a different combination of triangles connecting the points. Figure 6A is the "best" solution, which has the lowest FOM value (607.2). The figure of merit (FOM) is simply the sum of the S parameter of all triangles used. The FOM for Figs 6B, 6C, and 6D are 618.4, 4698.8, and 4729.7, respectively. A and B were the two best triangle combinations based on the FOM score; C and D were the two worst among the several hundred solutions found.

capable of the correction of arbitrary, nonlinear inplane patient motion. Inplane motion here refers to linear and nonlinear translational or rotational motion, but not complex patient motions involving different superimposition of overlapping structures in the direction parallel to the x -ray beam, which generally cannot be corrected.

The piecewise correction or *warping* procedure makes use of triangular regions (triangles) strung between the N_{points} coordinate pairs (Fig 1). How the triangles are selected given the spatial positions of the N_{points} coordinate pairs is described in the following section. Here, the warping algorithm is described assuming that a pair of triangles has been selected; one triangle on the contrast image is strung between three (primed) coordinates on that image $[(x'_1, y'_1), (x'_2, y'_2) \text{ and } (x'_3, y'_3)]$, and another corresponding triangle on the mask image is defined from the three (unprimed) corresponding points $[(x_1, y_1), (x_2, y_2) \text{ and } (x_3, y_3)]$ on that image. The equations used to warp the image inside the triangle are:

$$x' = \alpha_x + \beta_x x + \epsilon_x y \quad (2A)$$

$$y' = \alpha_y + \beta_y x + \epsilon_y y \quad (2B)$$

The values of the coefficients α , β , and ϵ in equations 2A and 2B are solved algebraically. The x transformation coefficients are given by:

$$\epsilon_x = \frac{x'_1(x_3 - x_2) + x'_2(x_1 - x_3) + x'_3(x_2 - x_1)}{x_1(y_2 - y_3) + x_2(y_3 - y_1) + x_3(y_1 - y_2)} \quad (3A)$$

$$\beta_x = \frac{x'_2 - x'_1 - \epsilon_x(y_2 - y_1)}{x_2 - x_1} \quad (3B)$$

$$\alpha_x = x'_1 - \beta_x x_1 - \epsilon_x y_1 \quad (3C)$$

The y transformation coefficients are given by:

$$\epsilon_y = \frac{y'_1(x_3 - x_2) + y'_2(x_1 - x_3) + y'_3(x_2 - x_1)}{x_1(y_2 - y_3) + x_2(y_3 - y_1) + x_3(y_1 - y_2)} \quad (4A)$$

$$\beta_y = \frac{y'_2 - y'_1 - \epsilon_y(y_2 - y_1)}{x_2 - x_1} \quad (4B)$$

$$\alpha_y = y'_1 - \beta_y x_1 - \epsilon_y y_1 \quad (4C)$$

The coordinate transform given in equations 2A and 2B results

Fig 7. (A) A digitally subtracted neuroangiogram without warp registration. With the modest amount of motion between the subtraction pairs, this image is already acceptable. (B) The effect of the image warping to correct for misregistration; improvement is seen over the unwarped subtraction.

in noninteger values of x' and y' , whereas the real image is defined only at integer pixel values on the (x', y') plane. Therefore, bilinear interpolation is used. Referring to the symbol definitions given in Fig 2, the pixel value (P) (or gray-scale value) at a location $P(x', y')$ is given by the distance-weighted sums of the closest four pixel values:

$$P(x', y') = a P(ix, iy) + b P(ix + 1, iy) + c P(ix, iy + 1) + d P(ix + 1, iy + 1) \quad (5)$$

where:

$$a = (1 - \Delta_x)(1 - \Delta_y) \quad (6a)$$

$$b = \Delta_x(1 - \Delta_y) \quad (6b)$$

$$c = (1 - \Delta_x)\Delta_y \quad (6c)$$

$$d = \Delta_x\Delta_y \quad (6d)$$

The warping transformation operation is performed in a similar manner for all the selected triangles in the image. For a given pixel on the image to be warped, there are numerous ways to choose the three point pairs required for generating the warping coefficients (α, β, ϵ). For example, one may choose the closest three coordinate pairs. However, the closest three coordinate pairs to a given pixel on an image often will define a triangle that does not contain that pixel. Experience with this warping algorithm has shown that pixels must be warped within strict triangular boundaries to achieve seamless warping across the entire image. In other words, the warping coefficients to be used for a given pixel on the image should be produced by the three points that define a triangle that encloses that point. However,

there are many ways to select the placement of triangles among the coordinate points, and this is discussed below.

Triangle selection. For a set of N_{points} on the image, the theoretical number of triangles using all possible connections between points is $N_{\text{tri}}^* = N(N - 1)(N - 2)$, where the asterisk indicates the theoretical value. Because of this near-cubic expansion, it is necessary for computational efficiency to reduce the number of triangles where possible. Since the warping algorithm described above should prudently use the smallest enclosing triangle in which to calculate the warping parameters, triangles with points inside them can be eliminated. Consequently, while all N_{tri}^* possible triangle configurations were calculated, each triangle was evaluated to see if any of the other $(N_{\text{points}} - 3)$ points fell within its boundaries. If a triangle was found to have one or more points within its interior, that triangle was eliminated as a candidate for the warping algorithm. This exclusion criterion was examined for its ability to reduce the number of candidate triangles, with results illustrated in Fig 3. A reduction of nearly an order of magnitude in the number of triangles was accomplished, such that the theoretical number of triangles, N_{tri}^* , was reduced to the effective value, denoted N_{tri} .

Experience with the warping algorithm described above and common sense suggest that the triangles used for warping should be as small as possible and as close to equilateral as possible. The elimination of triangles with internal points is a step toward selecting the smallest triangles possible. When highly skewed triangles are used in the warping algorithm, the shift values ($\delta x, \delta y$) from far distant coordinates inaccurately influence regional warping characteristics toward the center of the triangle. Therefore, triangles that differ significantly from

Fig 8. Marked misregistration is seen in A, between the two digitized film images from an angiographic sequence obtained near the ankle. After efforts to register the images (B), much better subtraction was realized.

equilateral (*skewed* triangles) are to be avoided whenever possible. To do this, a parameter related to the skewness of a triangle, referred to as the skew coefficient S , was defined as:

$$S = \frac{(\text{perimeter})^2}{\text{area}} - S_{\text{equilateral}} \quad (7)$$

The value of $S_{\text{equilateral}}$ is $(9 \times 4 \times 3^{-1/2} = 20.7846)$. Figure 4 shows several triangles and their corresponding skew coefficients. The skew coefficient S is independent of the absolute *size* of the triangle—it is dependent only on the triangle *shape*.

At this point, N_{tri} triangles have been selected, and the skew parameter is known for each. Given an array of points that overlies an image, as illustrated in Fig 5, we sought to connect these points using a set of nonoverlapping triangles. Optimally, the set of triangles used to connect all the points in the image would be made up of triangles with low skew parameters; however, an analytical method for determining the best set of triangles from the N_{tri} possible ones probably does not exist. Consequently, an iterative solution for finding the optimal configuration of triangles was used.

For the sake of description, the concept of a list Λ is introduced. Λ is a list containing N_{tri} triangles, but the order of the list is a variable. For the first iteration, the N_{tri} triangles were rank-ordered by skew parameter, so that triangles with the lowest S values were at the top of the list. Subsequent iterations

were invoked, which used a different ordering of the list (described below), and let us define a list Λ_i for iteration i . An algorithm (referred to as the *triangular placement* algorithm) was written, which stepped through each triangle in the list from top to bottom in order. Given a list Λ_i , the first triangle at the top of the list is always accepted. The algorithm then checks the second triangle to see if it overlaps the first; if it does, this second triangle is rejected. Triangles may make use of the same endpoints, and it is even possible for two triangles to share two common endpoints and not overlap. The algorithm continues to evaluate each subsequent triangle in the list, verifying that overlap with all previously accepted triangles does not occur. Once the list has been examined completely (once), the area defined by all outermost points (white line in Fig 5) will be filled completely. Therefore, with each iteration throughout the list, a solution consisting of a combination of nonoverlapping triangles is found, and this combination of triangles is a subset of the N_{tri} triangles. The sum of the S values of all accepted triangles is calculated for each iteration, and this sum is defined as the figure of merit (FOM_i). To explore other solutions, the list is pseudorandomized, the triangular placement algorithm is run, and the FOM_i for iteration i is calculated. A solution set of triangles with the lowest FOM should be close to the optimal set.

The order of the list will determine the way in which the area on the image gets filled with triangles, and thus the order varies

with each iteration. Although complete randomization of the list with each iteration is one possible approach, this was examined and found not to result in optimal solutions as demonstrated by higher values of FOM. Rather than complete randomization, a slight shuffling of the list was performed. By randomizing the order of the triangles only slightly, the best triangles would still be placed initially and the less optimal (higher S parameter) ones would be placed only as a last resort, to fill in "holes." The *shuffling algorithm* shuffled the list Λ a total of $2N_{tri}$ times; however, the results were relatively insensitive to this number. The shuffle procedure that was performed $2N_{tri}$ times per iteration consisted simply of selecting one triangle in the list and swapping its rank in the list with a triangle that was in the M position in the list. M was variable, such that $M = 1$ (ie, shuffling adjacent triangles in the list) for the first 100 iterations, $M = 5$ for the second 100 iterations, and $M = 10$ for the third 100 iterations. A total of 300 iterations were used. Certainly there are many other ways to slightly reorder the triangles in the list that would yield adequate results. The combination of triangles that resulted in the lowest FOM of the 300 FOMs calculated was selected for the warping algorithm.

RESULTS

Figure 6 illustrates four different possible ways to place triangles on the array of points shown in Fig 5. Figure 6A shows the best combination of triangles as determined by the lowest FOM, at 607.2. Figure 6B shows the second-best combination, with an FOM of 618.4. Figures 6C and 6D

demonstrate the two worst combination of triangles, with FOM values of 4,698.8 and 4,729.7, respectively. Figures 6C and 6D have more highly skewed triangles. The point in the upper left corner of both these figures appears unconnected, but is it connected with the neighboring points to the left and right in a very highly skewed triangle.

Figure 7 illustrates a neuroangiogram with crude registration on the left (7A) and after warp registration on the right (7B). As expected, better subtraction is achieved after the warping operation.

Figures 8 and 9 were obtained from the same angiographic film pair. Figure 8 shows the more proximal anatomy; figure 9 demonstrates the more distal aspects of the foot. The left image in both figures (8A and 9A) is the crudely registered subtraction; the images on the right (8B and 9B) show the subtracted images after the warp registration procedure.

DISCUSSION

Despite the clinical success and utility of intraarterial digital subtraction angiography, some angiographic examinations require the spatial resolution that, at present, only film subtraction can provide.

Fig 9. (A) Slight misregistration between views on this subtraction almost completely obscures the artery on this angiogram of the lower extremity. After warp registration, the subtraction image showed much better vessel detail.

The use of digital subtraction from the digitized films may result in higher quality subtraction images, which can be produced faster and less expensively. Although there are sizable up-front costs, as mentioned by Kofler et al,² film digitizers and computers are becoming more and more commonplace in radiology departments. Because the proposed technique does not require a film processor after initial processing of the film angiograms, it may be a practical alternative for use in the angiographer's reading area or office, which may be far from the film processing areas. The digital subtraction technique also represents an easy way to produce subtractions from archived angiographic studies in which subtraction films originally were not made.

An additional benefit of performing the subtraction procedure digitally is that digital analysis software³ can be used for the display of images. While simple windowing and leveling of digital images are no longer considered sophisticated, this technique can markedly increase image contrast and can have striking results in terms of image presentation. Because the resulting subtraction image produced from the technique described here is in digital format, analytical techniques such as the evaluation of vessel characteristics⁴⁻⁸ and calculation of vascular flow^{7,9} can be employed. The digitization of the original film images and generation of digital subtraction images also may serve as an entry point for these images into a digital imaging network and archive system.

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