In Vitro Modeling of Spinal Anesthesia

A Digital Video Image Processing Technique and Its Application to Catheter Characterization


Background: Maldistribution of intrathecal local anesthetic has recently been implicated as a contributor to neurotoxic injury. In vitro modeling can be used to understand the distribution of anesthetic agents within the subarachnoid space. We describe an in vitro modeling technique that uses digital video image processing and its application to catheter injection of local anesthetic.

Methods: A clear plastic model of the subarachnoid space, including a simulated spinal cord and cauda equina, was filled with lactated Ringer's solution. Phthalocyanine blue dye of known concentration was injected into the model through small-bore (28-G) and large-bore (18-G) catheters. Injections were performed at a variety of controlled rates and sacral catheter positions, and the propagation of dye throughout the model was recorded on videotape, digitized by computer, and converted to a two-dimensional image of dye concentration. A subset of data was compared with results obtained from spectrophotometric analysis.

Results: There was a strong correlation ($r = 0.98$) between data obtained with analysis by digital video image processing and those obtained spectrophotometrically. Catheter size, catheter angle, and injection rate significantly influenced the distribution and peak concentration of simulated anesthetic.

DISTRIBUTION of local anesthetic within the subarachnoid space is a critical determinant of successful spinal anesthesia. In addition, there is evidence to suggest that local anesthetic maldistribution may, at times, contribute to anesthetic-induced neural injury. In vitro modeling can be used to investigate the factors that affect distribution of anesthetic within the subarachnoid space. Modeling has its origins in the work of Barker who, in 1907, injected solutions colored with methyl violet into 0.5-inch glass tubes bent to the shape of the spinal curvature. Recently, since reports of cauda equina syndrome after continuous spinal anesthesia, investigators have used in vitro models to perform qualitative and quantitative studies of catheter-injected local anesthetic. In these quantitative studies, anesthetic distribution was determined by sampling the contents of the model at discrete points, measuring the dye absorbance spectrophotometrically, and then calculating the corresponding dye concentration. Although these techniques can accurately quantify distribution, considerable effort is required to obtain the samples and determine the respective dye concentration. Further, the methodology is limited to several discrete locations in the model and, in general, to one time point during the simulated injection. In addition,
withdrawal of the samples may disturb the distribution of dye within the model.

This paper discusses a methodology to overcome these limitations. The technique described uses digital video image processing (DVIP) to quantify the flow and distribution characteristics during simulated spinal injection. The technique eliminates the need for direct fluid sampling and can generate a two-dimensional map of distribution at any time during injection. Application of this technique is demonstrated by evaluating the effect of catheter size, catheter position, catheter type, and injection rate on dye distribution.

Materials and Methods

Model

The spinal model was constructed as previously described but was modified to include a simulated spinal cord consisting of a 1-cm (outside diameter) Tygon tube and sacral rootlets simulated by ten pairs of polyethylene tubing (PE20, Becton Dickinson, Parsippany, NJ), 2 mm in outside diameter and 20 cm in length. The model was 18 mm in inner diameter, 25 mm in outer diameter, and 66 cm in length. The distal 5 cm was machined to approximate the sacral taper, and a dorsal injection port was positioned between the simulated L3 and L4 spinous processes (fig. 1).

The model was filled with lactated Ringer's solution (specific gravity 1.005). The simulated anesthetic injectate (specific gravity 1.047) was composed of distilled water containing 7.5% dextrose and 0.84% (840 mg/l) phthalocyanine blue dye (Aldridge Chemical, Milwaukee, WI), which is visible by the DVIP method yet stable under fluorescent back illumination. All injections were performed with the model and injectate at room temperature and in the horizontal supine position. Room temperature injectate disperses in vivo before warming to body temperature; therefore the test injectate baricity was adjusted for thermal density differences. The injectate baricity (1.047) was chosen to ensure that the relative density difference (on which the buoyancy force depends) between cerebrospinal fluid and injectate was the same in the simulations as in the in vivo setting. The value of the relative density difference, approximately 4%, was based on the maximum anesthetic density used clinically, 1.037 g/ml (for 5% lidocaine and 7.5% dextrose), and the minimum cerebrospinal fluid density (1.000 g/ml at 37°C).

Injection

The injections were performed with a programmable syringe pump (model 2304, Harvard Apparatus, Boston, MA). To view the injection process, the model was back-lit with a uniform fluorescent lightbox. Video recording began 1 min before injection and was continued for 4–6 min after completion. After each trial, the model was drained, refilled with fresh Ringer's solution, and repositioned for the next injection.

Digital Video Image Processing

Preinjection and postinjection video images of the model were digitally captured and the artifacts minimized by digital subtraction (fig. 1). The subtracted images were then analyzed by comparing light-intensity levels in the model with calibrated concentration values.

Image and Data Analysis

Images were analyzed by CATHIMG, an image processing program developed in-house with Turbo Pascal 5.5 (Borland International, Scotts Valley, CA). Light is

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‡‡ This program is available free of charge by contacting Sandy F. C. Stewart, Ph.D., Food and Drug Administration/Center for Devices and Radiological Health, 12721 Twinbrook Parkway, Rockville, Maryland 20852.

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VIDEO ANALYSIS OF SIMULATED SUBARACHNOID INJECTION

absorbed by the anesthetic-simulating dye but also to some extent by the spinal model itself (including the simulated spinal column and spinal rootlets). Artifactual light absorption by the model was minimized by digitally subtracting the preinjection image (without dye) from the postinjection image. The light absorption by the model is expected to be the same postinjection as preinjection. Therefore the subtraction removed contributions of light absorption by the model, leaving only that by the dye, which could then be read directly (in milligrams per liter) from the image. Figure 2 shows the digital postinjection images and the subtracted images for 2-s and 10-s 1-ml injections through an 18-G catheter.

The image intensities were calibrated with six vials filled with various known dye concentrations by fitting a piecewise linear function between the known dye concentration (in milligrams per liter) and the average light intensity in each vial. Artifact reduction was done before the calibration step by digitally subtracting a stored image of a seventh, Ringer's-filled vial (that is, without dye) from each dye-containing vial. In this way, errors introduced by light absorption by the walls of the vials also were minimized. The vials were made of the same tubing material as the spinal model to duplicate the light-absorbing characteristics of the model.

Part of the analysis depended on digital integration of the dye concentration on rectangular subsets of the spinal model image. These digital integrations allowed a simpler method of artifact reduction. In this case, the integrations were calculated on the initial, preinjection image and then subtracted from those derived from the final postinjection image. Thus any contribution to the integral by light absorption from the model, which would be expected to be the same postinjection as preinjection, was removed by the subtraction.

Three types of quantitative analysis were performed. In the first analysis, peak concentrations, defined as the maximum pixel (picture element) value, were determined from subtracted images as shown in figure 2. In the second and third types of analysis, digital integrations were used. The image was divided into two rectangular subsets, one sacral and one cephalad, split at the origin where the catheter entered the model. The sacral/cephalad (S/C) dye ratio, defined as the ratio of the total amount of dye in each part, was calculated from the two integrals (as corrected by the initial, dye-free image). Finally, integrals were performed on 20 rectangular subsets along the x-axis (again corrected by the subtraction of the initial, dye-free image) to provide dye concentration as a function of axial position.

Digital Video Image Processing Quantification and Validation

The concentration of dye measured by DVIP was compared with that measured by a spectrophotometric

Fig. 2. Postinjection model images for 2-s (A) and 10-s (B) injection through an 18-G catheter angled 80° sacrally. Subtracted dye images for 2-s (C) and 10-s (D) injection through an 18-G catheter angled 80° sacrally.

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method.\textsuperscript{5,6} The sampling was performed with the same calibration vials and injection solution as had been used with DVIP and was videotaped for later analysis by DVIP. A model containing 24 sampling ports on the inferior or dorsal side was placed in the supine horizontal position and filled with lactated Ringer’s solution. A 25-G needle was passed through the port corresponding to the L3–L4 interspace, positioned perpendicular to the ventral surface of the model, and 1 ml dye-containing solution was injected manually over an approximately 1-s period. Three minutes after injection, starting at the caudal end, 0.1 ml fluid was aspirated from every other port on the dorsal side of the model (12 samples per trial). The absorbance of the aspirated samples was measured with a spectrophotometer (model DV-64, Beckman Instruments, Anaheim, CA). Absorbance measurements were made at 610 nm, which corresponds to the peak sensitivity for phthalocyanine blue dye.

To relate absorbance and dye concentration, each of the calibration vials used for the DVIP method was measured spectrophotometrically. Four trials were performed and recorded on videotape by the same protocol. Quantitative single-point determinations were made by DVIP analysis manually by placing the cursor at the same aspiration sites as the spectrophotometric sampling technique. Path length corrections in the sacral tip area were implemented in the software and were used for these single-point measurements and for other average and peak dye concentration measurements in the sacral tip area.

\textbf{Catheter Flow Characterization}

The DVIP method was used to assess the flow characteristics of three commercial catheters (28-G, Kendall Co-Span, Mansfield, MA; 28-G, Preferred Medical Products, Thorold, Ontario, Canada; and 18-G, Burron Medical, Bethlehem, PA). The catheter orientation was described in terms of angle of the catheter with respect to the model, where 0° represented a sacrally directed catheter parallel to the long axis of the subarachnoid space and 90° represented a catheter perpendicular to the ventral surface of the model. The actual measured catheter angle varied between 58° and 87°.

For each of the three catheters tested, at least three trials were performed at two catheter positions (more sacral and less sacral) and at two injection rates (fast and slow). Measured angles, adjusted for refraction, were recorded for each trial. Injection flow rates for the 28-G catheters were 3 (fast) and 1 (slow) ml/min. The 18-G catheter injection parameters were 30 (fast) and 6 (slow) ml/min. The fast rates represented the maximum injection rates possible with the syringe pump, and the slow rates were estimated to represent the extremes of clinically relevant rates.\textsuperscript{5} The dye distribution ratio S/C and peak sacral dye concentration were determined as a function of catheter angle, injection rate, catheter size, and catheter type. Dye dispersion data were mapped in detail in the form of histograms of dye concentration as a function of axial position. Direct measurements of the jet velocities from the three test catheters were made with small hot-film anemometry probes. Measurements were made 1 mm from the catheter face at each of the flow rates being examined.

Analysis of variance was performed with peak concentration and S/C ratio as dependent variables. Four independent variables were used: size of the catheter (large bore [18-G] \textit{vs.} small bore [28-G]), catheter type (Kendall \textit{vs.} Preferred), measured angle (58° to 87°), and injection rate (fast \textit{vs.} slow).

\textbf{Results}

\textbf{Digital Video Image Processing Method Validation}

When dye concentration determined by DVIP was compared with that obtained by spectrophotometric analysis, the maximum error at a sampling port was 15\% (fig. 3), and the correlation coefficient between the two data sets was 0.98. A 10\% variation in dye concentration was measured by DVIP for a model filled with constant dye concentrations of 20 or 160 mg/l (fig. 4).

\textbf{Catheter Flow Characterization}

\textbf{Jet Velocities.} At a maximum flow rate of 3 ml/min, hot-film anemometry showed peak jet velocities of 139.5 \pm 0.2 cm/s for the Kendall, 178.1 \pm 0.2 cm/s for the Preferred, and 29.0 \pm 0.2 cm/s for the Burron 18-G catheter at a distance of 1 mm from the hot-film probe. The inner diameter for the two 28-G catheters was 180 \textmu m and for the 18-G catheter was 470 \textmu m. Theoretical calculations for jet velocities for comparable tubes of inner diameter 180 and 470 \textmu m were 195 and 30 cm/s respectively, according to bulk-flow calculations (v = Q/\Delta, where v = jet velocity; Q = injection rate; and \Delta = tube area).

\textbf{Model Distribution.} A subset of 17 trials for the 18-G and 28-G catheters at similar angles (74° \pm 2°)
showed that catheter size had a strong effect on both the peak concentration and the S/C ratio (table 1).

In the comparison of the two 28-G catheters (27 trials), only the measured catheter angle significantly affected both peak concentration and S/C ratio (table 2). The dependence of peak concentration on angle is displayed in figure 5, which shows the best-fit lines for both the Kendall and Preferred catheters (r = 0.91 for Kendall and 0.92 for Preferred). The range of measured peak dye concentration varied from 48 to 437 mg/l for all 39 injection trials, which corresponds to a range of fraction of injectate of 0.06–0.52. According to these results, if 5% lidocaine were used as the injectate, corresponding peak lidocaine levels would be 0.3–2.6%. Catheter type (Kendall vs. Preferred) had no significant effect on peak dye concentration or S/C ratio (table 2), and injection rate had a significant effect only on the S/C ratio.

Analysis of injection rate for the 18-G catheter showed that distribution was significantly more uniform in the sacral tip with the fast injection than with the slow. The more uniform concentration field for the fast rate can be seen in figure 6 and qualitatively in figure 2. For the 18-G catheter only injection rate had a significant effect on peak concentration (table 3), and only measured angle had a significant effect on the S/C ratio.

**Table 1. Peak Concentration and S/C Ratio Versus Size for Similar Angles (74° ± 2°)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SEM)</th>
<th>P</th>
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<tbody>
<tr>
<td>Peak concentration (mg/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 G</td>
<td>104 (21.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>28 G</td>
<td>335 (14.0)</td>
<td></td>
</tr>
<tr>
<td>S/C ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 G</td>
<td>1.66 (0.604)</td>
<td>0.029</td>
</tr>
<tr>
<td>28 G</td>
<td>3.42 (0.392)</td>
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**Discussion**

The DVIP technique can be used to quantify anesthetic distribution within a model of the subarachnoid space. This method has numerous advantages over previous techniques. With the DVIP method, a single in-

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Table 2. Peak Concentration and S/C Ratio Versus Angle, Rate, and Catheter Type for 28-G Catheters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SEM)</th>
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<tr>
<td>Peak concentration (mg/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection angle Fast</td>
<td>248 (13.9)</td>
<td>0.506 (NS)</td>
</tr>
<tr>
<td>Slow</td>
<td>261 (13.4)</td>
<td></td>
</tr>
<tr>
<td>Injection rate Kendall</td>
<td>251 (12.1)</td>
<td>0.555 (NS)</td>
</tr>
<tr>
<td>Preferred</td>
<td>254 (11.6)</td>
<td></td>
</tr>
<tr>
<td>S/C ratio Injection angle Fast</td>
<td>2.06 (0.461)</td>
<td>0.0025</td>
</tr>
<tr>
<td>Slow</td>
<td>3.59 (0.444)</td>
<td></td>
</tr>
<tr>
<td>Catheter type Kendall</td>
<td>2.28 (0.366)</td>
<td>0.310 (NS)</td>
</tr>
<tr>
<td>Preferred</td>
<td>3.19 (0.351)</td>
<td></td>
</tr>
</tbody>
</table>

NS = not significant.
* Not applicable for continuous variable.
† 28 G: fast = 20 s, slow = 60 s.

The injection experiment requires approximately 5 min, and analysis can be completed within approximately 30 min. In contrast, techniques dependent on sampling require several hours for withdrawal of samples, measurement of absorbance, and calculation of dye concentration from spectrophotometric data. The DVIP method also provides a two-dimensional map of dye concentration rather than several discrete point measurements and thereby vastly increases the amount of information available from each experiment. In addition, because the entire injection is recorded on videotape, data are available for any time point during the experiment and need not be analyzed at the time of the injection. The DVIP method provides quantitative information without withdrawal of solution for analysis, thereby eliminating potential sampling and extraction artifacts.

Furthermore, the elimination of sampling ports removes a major barrier to the development of flexible, more anatomically correct models. Although results are presented as a two-dimensional map, the plane of reference could be rotated merely by movement of the camera and light source. In addition, multiple two-dimensional analysis could be performed. Thus, there is the potential for integration of multiple planes to construct three-dimensional images. In contrast, the spectrophotometric technique uses fixed sampling positions, imposing a considerable obstacle to alterations in spatial orientations.

We did not administer local anesthetic but instead used phthalocyanine blue dye. However, two previous spectrophotometric studies, which made measurements directly or with radiolabeled lidocaine, demonstrated a strong correlation between distribution of methylene blue dye and local anesthetic.

The accuracy of the DVIP technique was assessed by comparison with data from spectrophotometric analysis. The results of the two methods agreed extremely well, despite the difficulty in measuring with DVIP at the same sampling sites used by the spectrophotometric method, the inherent nonlinearity of the image, residual artifacts, and superposition of the third dimension. Finite-element computer simulations currently underway provide further corroborating evidence of the accuracy of the DVIP method.

Three catheters were studied. Twenty-eight-gauge catheters were chosen because the majority of cases of cauda equina syndrome after continuous spinal anesthesia (CSA) reported to the Food and Drug Administration involved the use of a small-bore catheter. Two types of 28-G catheter were studied to investigate if the differences

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in reported incidence of cauda equina syndrome associated with various small-bore catheters might be explained on the basis of differences in anesthetic distribution. Although of similar size, differences in configuration (such as variation in internal diameter or tapering of the tip) that may occur during manufacture might alter anesthetic distribution. An 18-G catheter was selected because it is the largest-gauge epidural catheter in common use and therefore may be used for continuous spinal anesthesia after deliberate or inadvertent subarachnoid placement. (It is likely, however, that 20-G catheters are more frequently chosen for large-bore—catheter continuous spinal anesthesia.)

When comparing 18-G and 28-G catheters at similar angles, we found that catheter size had a statistically significant effect. Greater size resulted in lower peak concentration and a lower S/C ratio. These reductions may occur because for a larger catheter, the amount of recirculating anesthetic (that which exits the catheter and is eventually entrained back into the catheter jet) is larger and the sacral flux of anesthetic therefore smaller.

When analyzing injections through the 18-G catheter alone, we found that only the injection rate significantly affected the peak concentration, whereas only the catheter angle significantly affected the S/C ratio. The influence of injection rate on peak concentration but not S/C ratio with the 18-G catheter is perhaps related to the higher turbulence levels in the 18-G catheter at its higher flow rates. Enhanced turbulent mixing, which occurs on small scales of length, can spread local areas of high anesthetic concentration (and thereby lower the peak concentration value) but only weakly affects the large-scale mixing that determines the S/C ratio. This conjecture regarding the effect of turbulent mixing is consistent with the data observed for the 28-G catheters alone. For the 28-G catheters, the flows were laminar rather than turbulent, and increasing the flow rate did not result in increased turbulent mixing and lower peak concentrations. For the diameter of the 28-G catheter, the viscosity of water, and the flow rates used in this study, steady flows from the small-bore catheter are in the laminar regime.

For the 28-G catheters, we found that small changes in catheter angle significantly affected dye distribution and peak concentration. Catheters positioned in a more caudal direction (closer to 0°) were associated with increased sacral distribution and higher peak concentration.

In previous in vitro studies modeling subarachnoid anesthetic distribution, catheter size, injection rate, and catheter position were observed to affect the distribution of an injected solution. The results of the current study confirm and extend those findings. Whereas the previous study of catheter position compared distribution only in relation to sacral or cephalad orientation, our study demonstrates that even small changes in orientation of a sacrally directed catheter can have a profound effect. However, because the ranges of orientation angles and injection rates considered in the current study were small, any conclusions for angles or injection rates outside that range would require further validation.

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**Table 3. Peak Concentration and S/C Ratio Versus Angle and Rate for 18-G Catheters**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SEM)</th>
<th>P</th>
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<tbody>
<tr>
<td>Peak concentration (mg/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection angle</td>
<td></td>
<td>0.179</td>
</tr>
<tr>
<td>Injection rate†</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fast</td>
<td>67 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Slow</td>
<td>144 (5.3)</td>
<td></td>
</tr>
<tr>
<td>S/C ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection angle</td>
<td></td>
<td>0.0044</td>
</tr>
<tr>
<td>Injection rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast</td>
<td>2.54 (0.342)</td>
<td>0.463 (NS)</td>
</tr>
<tr>
<td>Slow</td>
<td>3.17 (0.350)</td>
<td></td>
</tr>
</tbody>
</table>

NS = not significant.
* Not applicable for continuous variable.
† 18 G: fast = 2 s, slow = 10 s.

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In addition, the current study directly compared distribution of anesthetic administered through two 28-G catheters. We found that catheter type (Kendall vs. Preferred) did not significantly affect peak concentration or S/C ratio, so that at comparable angles and injection rates the two types of catheter behaved similarly, despite small differences in exit jet velocities. This finding suggests that the differences in reported incidence in cauda equina syndrome associated with various 28-G catheters cannot be explained on the basis of differences in anesthetic distribution.

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References


