Vertebral arteries

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Abstract

During the investigation period, which lasted almost four months, we made a research of the vertebral arteries in the posterior part of the head in children. During this time we investigated the size, diameter and the blood flow in those arteries to make a model and a completed a system to simulate the vertebral arteries in the human head. We built the model with the real dimensions of the human arteries and used a mixture of 60% glycerin + 40% water to simulate blood because it had almost the same viscosity. We worked with a positive displacement pump that simulated the heartbeat with an amplitude and frequency similar to that of the heart. We also worked with photodetectors, which were the most important equipment of the experiment, for determining the concentration of drug (in our case we used dye) flowing through the probes and sending signals to a computer program that displays the results in the monitor. The process allows knowing the exact drug concentration (dye in this case) flowing through each artery. This approach has yet to be tested in animals to determine its usefulness.

Sinopsis

Durante el período de investigación, el cual duró casi cuatro meses, se les hizo una investigación a unos niños de las arterias vertebrales en la parte posterior de sus cabezas. Durante este tiempo se investigó el tamaño y el diámetro de las arteria y el flujo de sangre en ellas para desarrollar un sistema para simular las arterias vertebrales en los seres humanos. Se hizo un modelo con dimensiones iguales a las de las arterias humanas y se usó una mezcla de

60% glicerina + 40% de agua para simular la sangre porque tiene la misma viscosidad. Se usó una bomba para simular los latidos del corazón con una amplitud y frecuencia similar a la del corazón. También se usaron fotodetectores, los cuales resultaron la parte más importante del experimento para determinar la concentración de la droga (en nuestra simulación usamos tinte) que pasa por las sondas y luego enviar señales a una computadora para presentar los resultados en la pantalla. Esto se hace para saber la concentración exacta del medicamento en cada arteria. Este proceso nesecita probarse en animales para saber si funciona.

Introduction

Intra-arterial drug delivery can achieve a pharmacokinetic advantage of high tumor drug concentration with relatively low systemic exposure. This method may improve drug effectiveness if systemic toxicity is limited. Childhood brain tumors frequently occur in brain regions served by the vertebral arteries. The pediatric branch is interested in intra-arterial approaches to the posterior circulation, and there is reason to expect severe drug streaming in this setting. Proper intra-arterial drug delivery requires uniform distribution of infused drug solution to all arterial branches distal to the catheter tip. An appropriate infusion scheme avoids the potential streaming phenomena at catheter tips that result in nonhomogeneous delivery to the infused region. Engineers at the Biomedical Engineering and Instrumentation Program (BEIP) will fabricate a flow model of the posterior cerebral circulation to investigate methods of intra-arterial infusion in order to insure proper, homogenous delivery of drug to the desired target tissue.

Experimental procedure

When I arrived to BEIP, Dr. Robert J. Lutz, my supervisor, had already stated the problem statement of the project in which I was going to work. In the statement there were some instructions I had to follow. During my first weeks I started reading and looking for information in the library, journals, books and also on the Internet. We tried to find out how those arteries were going to look like and how those arteries work in the human body. We needed

to find out how many arteries there are in that region; we also needed to know the exact length, diameter and flow rate of those vertebral arteries in children. We found that children have seven different types of arteries in the back of the head: the basilar artery (BA), posterior cerebral artery (PCA), superior cerebellar artery (SCA), long and short pontine arteries, anterior inferior cerebellar arteries (AICA), posterior inferior cerebellar arteries (PICA) and vertebral artery (VA). We were interested in these arteries, especially the pontine and the AICA, and on how blood flows through these arteries because during childhood tumors are more frequent in that place. We searched for information on different books and research journals looking for experiments describing and giving measurement of those arteries. We found hundreds of studies with hundreds of measurement with different results. Eventually we took an average of the 14 branches and made the model with that average. Finally we obtained the diameter of each artery as table 1 shows.

Table 1. Diameter of each artery

Artery	Diameter (ϕ) inches	Diameter (ϕ) centimeters
BA	0.187	0.475
PICA	0.062	0.157
AICA	0.062	0.157
LSPA	0.031	0.0787
SCA	0.062	0.157
PCA	0.097	0.246
VA	0.156	0.396

After we found every diameter, we started looking for the flow rate (Q) of each artery. However, to find Q we needed to know the velocity of the blood in each artery. We used a device called Transcranial Doppler (TCD), which is an ultrasonic beam that penetrates the skull to measure the velocity of blood. Table 2 shows the results of those measurements.

Table 2. Velocity of each artery

Artery	Velocity (centimeters/second)
BA	41 ± 10
VA	38 ± 10
ICA	39 ± 9
PCA	40 ± 10
SCA	40 ± 10
LSPA	50 ± 10

The following equations describe the flow rate (Q) for those arteries. The parameter A is the cross-sectional area of each artery. Knowing that Q is an average we rounded the result for each artery.

$$Q_{VA} = V_{VA} * A_{VA}$$
$$Q_{VA} = 38\ cm/s * \frac{\Pi(0.39624)^2}{4} \quad (1)$$
$$Q_{VA} = 281.14 \approx 280\ ml/\text{min}$$

$$Q_{PCA} = V_{PCA} * A_{PCA}$$
$$Q_{PCA} = 40\ cm/s * \frac{\Pi\ (0.246)^2}{4} \quad (2)$$
$$Q_{PCA} = 114.42 \approx 110\ ml/\text{min}$$

$$Q_{ICA} = V_{ICA} * A_{ICA}$$
$$Q_{ICA} = 40\ cm/s * \frac{\Pi\ (0.157cm)^2}{4} \quad (3)$$
$$Q_{ICA} = 45.57 \approx 50\ ml/\text{min}$$

$$Q_{LSPA} = V_{LSPA} * A_{LSPA}$$
$$Q_{LSPA} = 50\ cm/s * \frac{\Pi(0.07874)^2}{4} \quad (4)$$
$$Q_{LSPA} = 14.61 \approx 10\ ml/\text{min}$$

$$Q_{SCA} = V_{SCA} * A_{SCA}$$
$$Q_{SCA} = 40\ cm/s * \frac{\Pi(0.1574cm)^2}{4} \quad (5)$$
$$Q_{SCA} = 47.745 \approx 50\ ml/\text{min}.$$

After finding all the diameters, flow rate and velocity, length of the artery and the distance between each artery we used AutoCad to design the mold. Then we sent it to the machine shop to make the model that figure 1 illustrates.

The mold was made by one of the mechanics in the machine shop of the BEIP. The material of the model was a polymer called polycarbonate (this is the name of a simple material seen every day and called "plastic"). After that we proceeded to create the model and assemble the system according to the procedure that figure 2 shows.

Fig 1

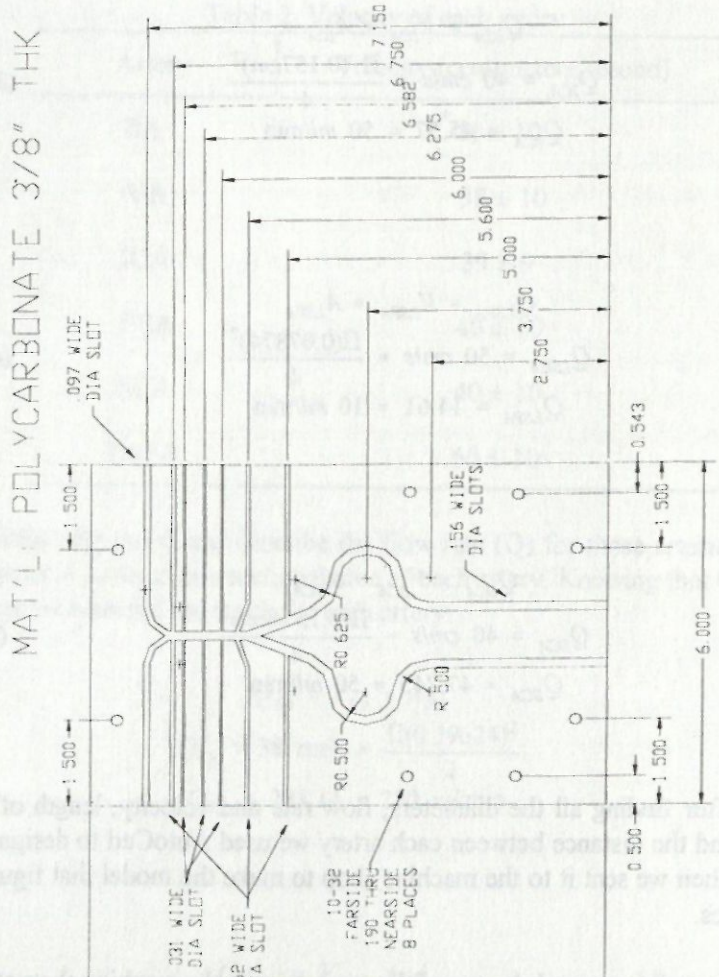

Figure 1. AutoCad rendition of the model

Fig. 2

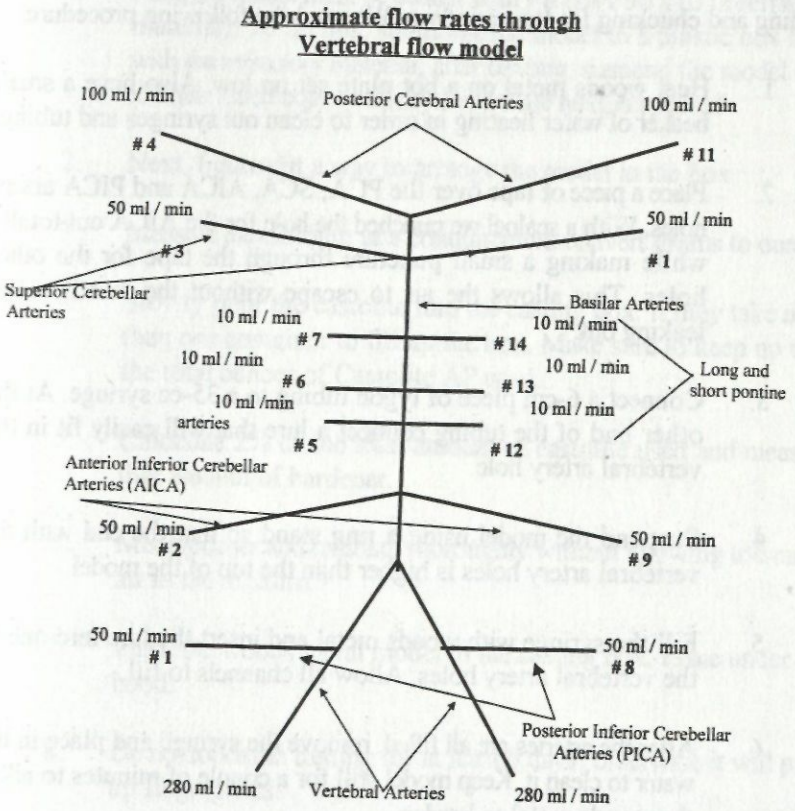

Figure 2. Procedure to create and assemble the system

Making the woods metal model

Next we needed to fill the model with the woods metal. Woods metal is an eutectic fusible alloy used, among other things for anchoring, filler for tube bending and chucking for lens grinding. We used the following procedure:

1. Heat woods metal on a hot plate set on low. Also have a small beaker of water heating in order to clean out syringes and tubing.

2. Place a piece of tape over the PCA, SCA, AICA and PICA artery holes. With a scalpel we punched the hole for the AICA out totally while making a small puncture through the tape for the other holes. This allows the air to escape without the woods metal leaking out.

3. Connect a 6-cm piece of tygon tubing to a 35-cc syringe. At the other end of the tubing connect a lure that will easily fit in the vertebral artery hole.

4. Suspend the model using a ring stand so that the end with the vertebral artery holes is higher than the top of the model.

5. Fill the syringe with woods metal and insert the lure into one of the vertebral artery holes. Allow all channels to fill.

6. After the arteries are all filled, remove the syringe and place in hot water to clean it. Keep model still for a couple of minutes to allow the woods metal to harden.

7. Take down the model and remove the screws. Slowly pry open the model using a spatula and slowly remove woods metal from model.

Then we had to to shape the model. This was done in a hot water bath. The model was slowly shaped to the desired form while in the water. We used

Castolite AP, Castolite hardener and Partall film #10 to cast the model according to the following procedure:

1. First, the model must be coated with Partall film #10 (a refractory material). To do this, submerge the model in a plastic box filled with the refractory material; after coating, suspend the model until it dries. Each coat must dry before the next is applied.

2. Next, figure out a way to arrange the model in the box.

3. Measure the castolite in a container and convert grams to ounces.

4. Slowly pour the castolite into the casting box. It may take more than one container to fill up the box. Make sure to keep up with the total ounces of Castolite AP used.

5. Calculate 2% of the total amount of castolite used and measure that amount of hardener.

6. Mix hardener and castolite thoroughly without allowing too much air in the mixture.

7. Place the woods metal model in the casting box. Place under the hood.

8. Do not touch the casting for at least 5 days; otherwise it will pick up fingerprints.

9. After 5 days, when the mold hardens, heat it a few degrees until the woods metal melts out.

To assemble the system we used the following equipment:

1. Six feet of tygon ½"
2. Centrifugal pump
3. Positive displacement pump

We had to create a pulsar movement like the heart's to simulate a real life environment. To have an amplitude similar to the real life heart we had to create a sinusoidal signal like the one in figure 3.

4. Tower
5. Deep platform
6. Glass connectors
7. Eight feet of tygon 1/8 "
8. 3" x 6" cylinder
9. Probes (photo-detectors)
10. Digital flow meter
11. Digital volt-meter
12. Box of 14 amplifiers
13. Oscilloscope

Finally,when all the system was completed, we started to set up the most important part of the research, the photo-detectors, with the help of Super-Scope II (a programmable instrument). The photo-detectors are semiconductor devices that transform light into an electric signal. This property was very helpful in our experiment. Fourteen photo-detectors were placed in the trajectory of the fluid to register the concentration of a number of light absorbing atoms or molecules. This information was sent later to a computer. In our experiment, instead of blood we used a mixture of ***60 % glycerin + 40% water***, which is almost the same density as blood.

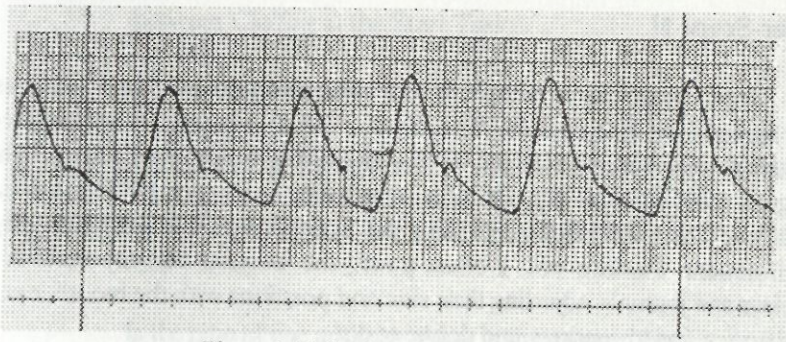

Figure 3. Behavior of a real life heart

After the system was all set up we applied the Beer's Law (a chemical engineering law used to determine the concentration of light absorbing species) to calculate the ratio of the power absorbed by the liquid.

The final equation of Beer's Law said:

$$Log \frac{P_0}{P} = \varepsilon * b * s = A \qquad (6)$$

In this case ε is the molar absortivity, b is the path length of the light of beam through the sample and c is the concentration of the compound solution. However, in this case we were interested only in the absorbance (A) to determine the concentration of drug passing through each artery.

It is in this stage when Super-Scope II comes into action. Before making any programming to calculate the wavelength of the signal, we first had to write the code for calibrating the system. The system needs calibration for checking whether all the 14 probes work correctly, because sometimes for some reason, the probes do not work correctly; and if it is not noticed all subsequent data are incorrect.

Super-Scope II

Super-Scope can be thought of as a combined word processor, database and spreadsheet program for waveforms. Waves are created, synthesized, digitized, analyzed, transferred, archived, edited, viewed and deleted. This program comes packed with a number of software "instruments." The user can modify or create new instruments using the Super-Scope II world-class design environment. Starting with a blank panel, the user can add any number of displays and journals, adjusting their size and positions with the mouse, create new waves, insert markers and define tasks.

Super-Scope II provides an easy to use environment by which the user explicitly defines acquisition, analysis, archival and presentation functionality. From this environment, the user defines little programs called tasks, which are easily created, deleted, and viewed with commands in the Task Menu. Commands under Task allow one to run a task, stop a running task, continue a stopped task, save a task to disk and load a task from disk.

The following is a description of the variables and parameters used in Super-Scope II.

- Cle = Clear

  We calculate the concentration of any number of molecules when the solution is clear to take it as a point of reference to later compare the change of power when the solution changes in color.

- Pink = Pink

  The solution becomes pink after we add ink to the system to calibrate it.

- Div = Division

  Is the boundary between Cle/Pink in the Calibrating Task and

between Cle/Sig in the Start Task.

- Abs = Absorvance

  Is the result of the Beer's Law and how much energy is absorved from the fluid. The equation is $\log_{10}$ (Div).

- Rat = Ratio

  Is the ratio of one arbitrary Abs (in this case is Abs#1) divided by the rest of the 13 photo-detectors.

- Conc = Concentration

  Is the product of Abs and Rat. With this we make the concentration equal to each photo-detector to correct any difference among them.

- B = Constant B = the product of Conc# * and variable Q#.

- Q# = Variable Q# = the volumetric flow of each artery.

- B_{total} = Variable B_{total} = the sum of each B constant.

- WellMix = Well Mix=B_{total}/ Q_{total}

- MI = Mixing Index = Con #/ WellMix.

Results

The following figures summarize the results obtained from the experiments

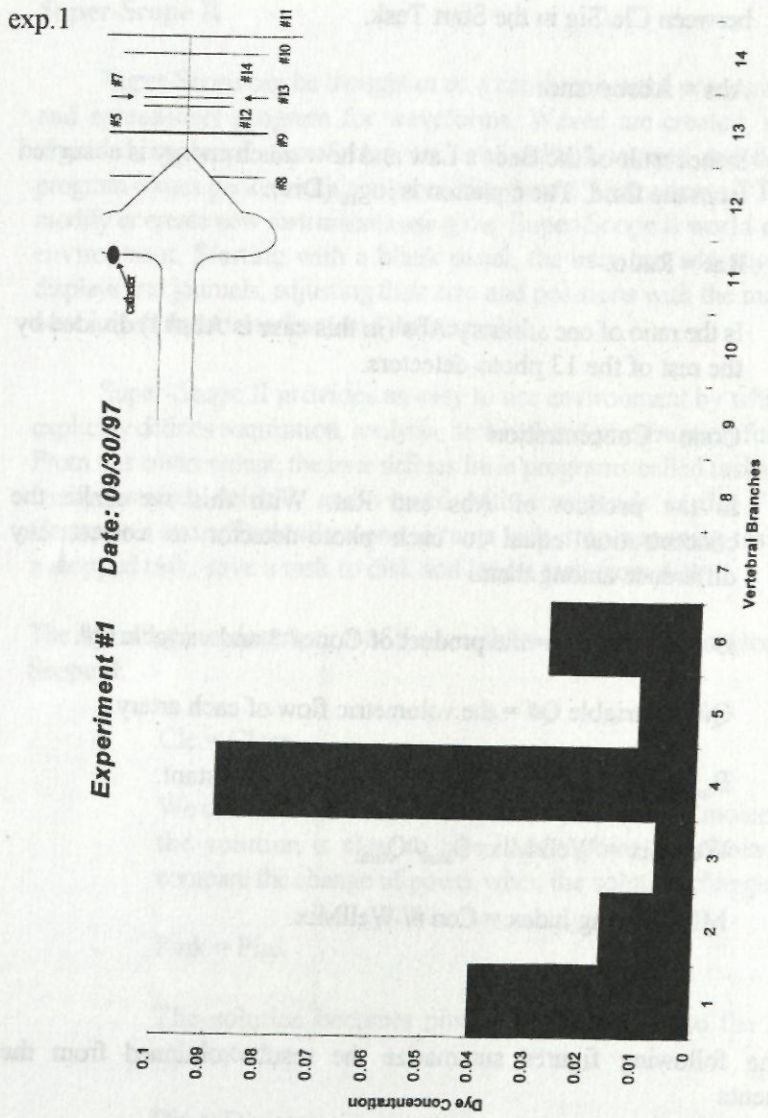

Figure 4. Results obtained from experiment 1

Exp. 2

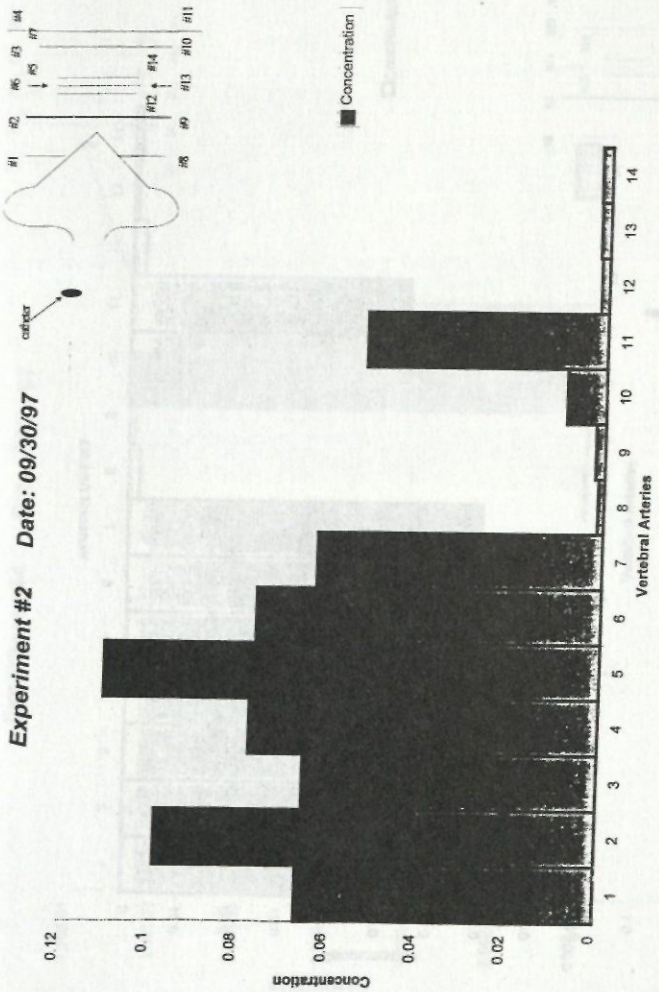

Figure 5. Results obtained from experiment 2

Exp 3

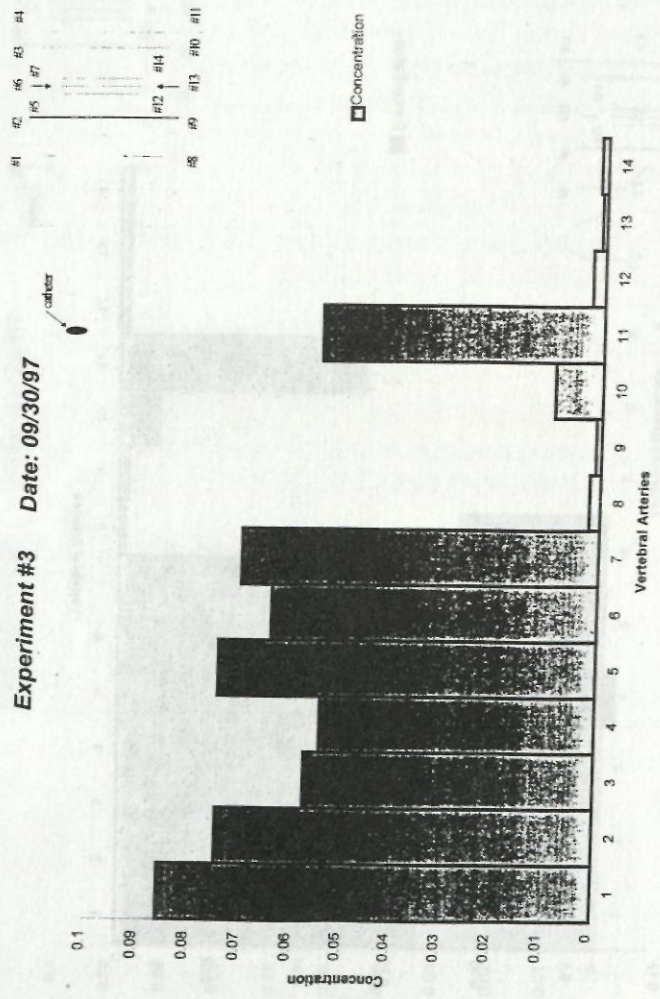

Figure 6. Results obtained from experiment 3

exp 4

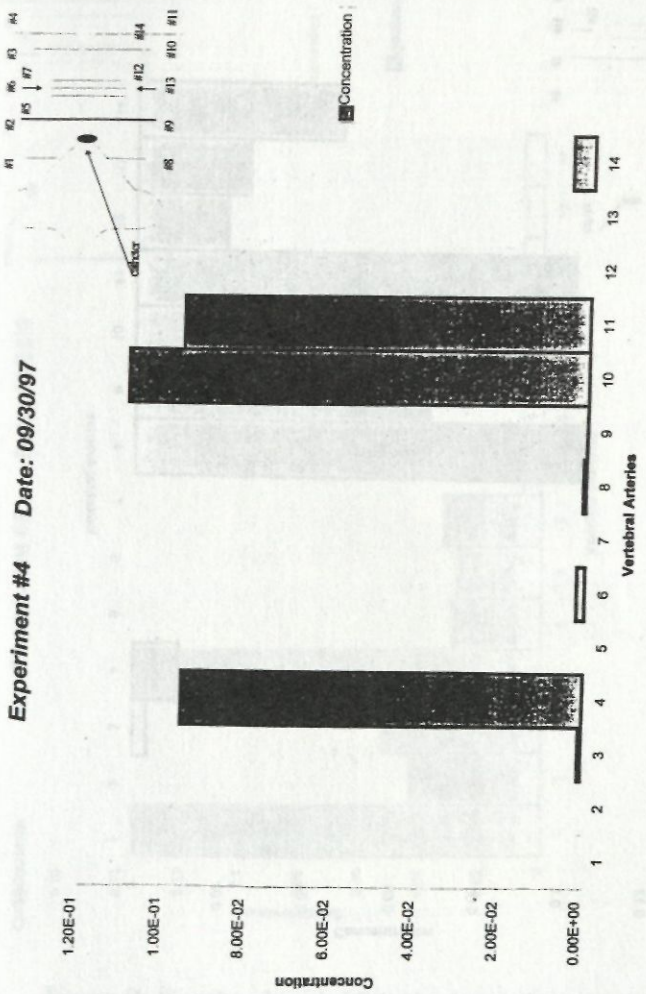

Figure 7. Results obtained from experiment 4

exp 5

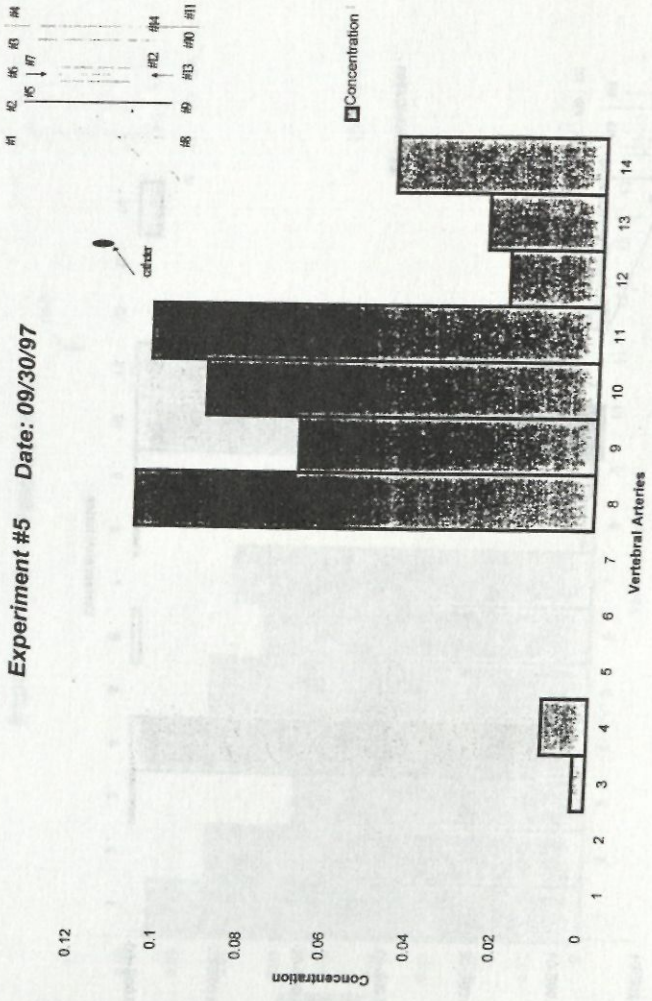

Figure 8. Results obtained from experiment 5

exp 6

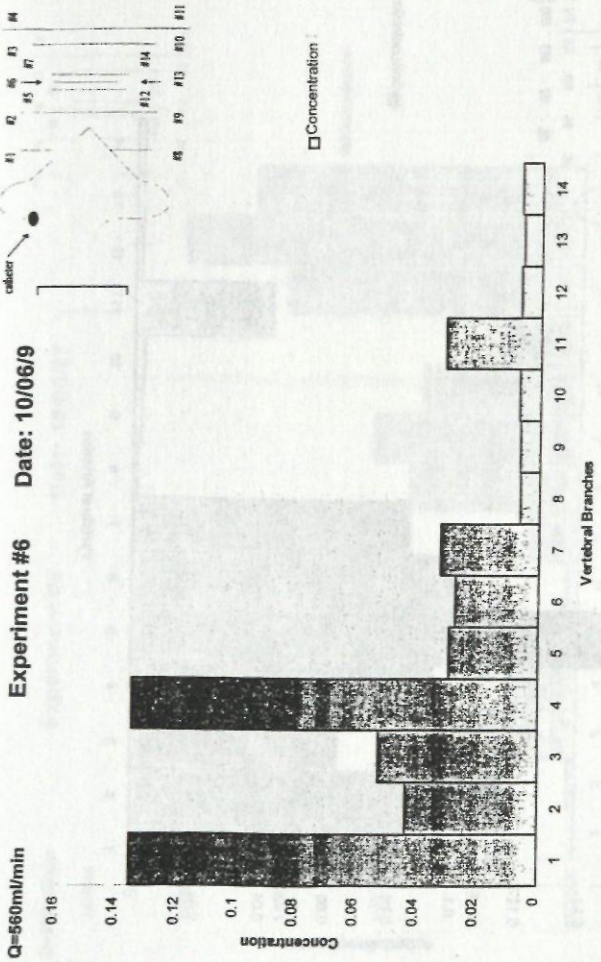

Figure 9. Results obtained from experiment 6

exp 7

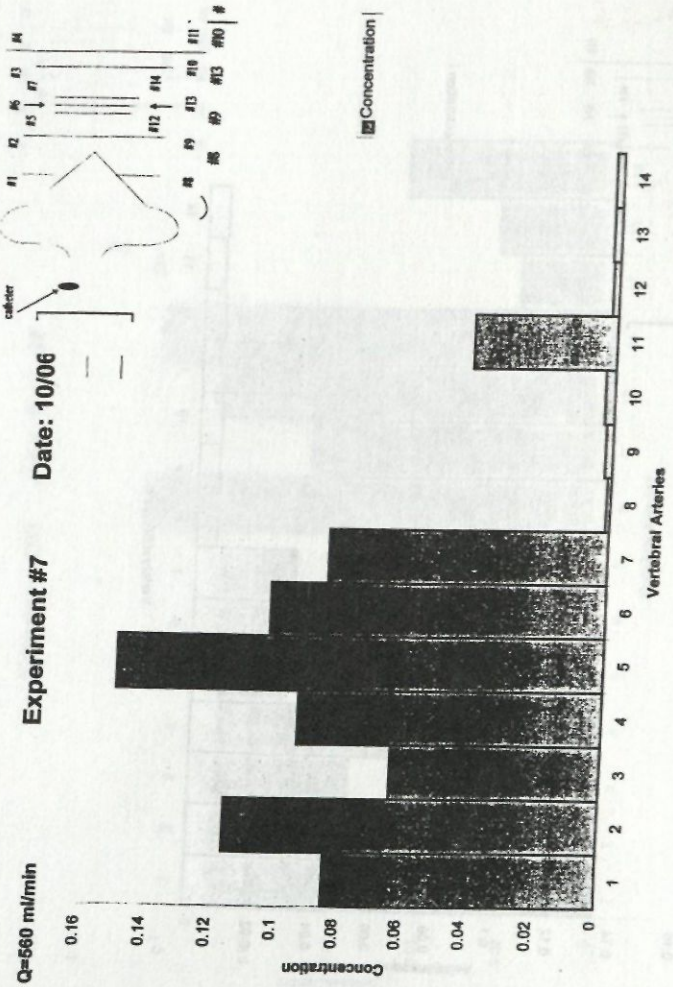

Figure 10. Results obtained from experiment 7

exp 8

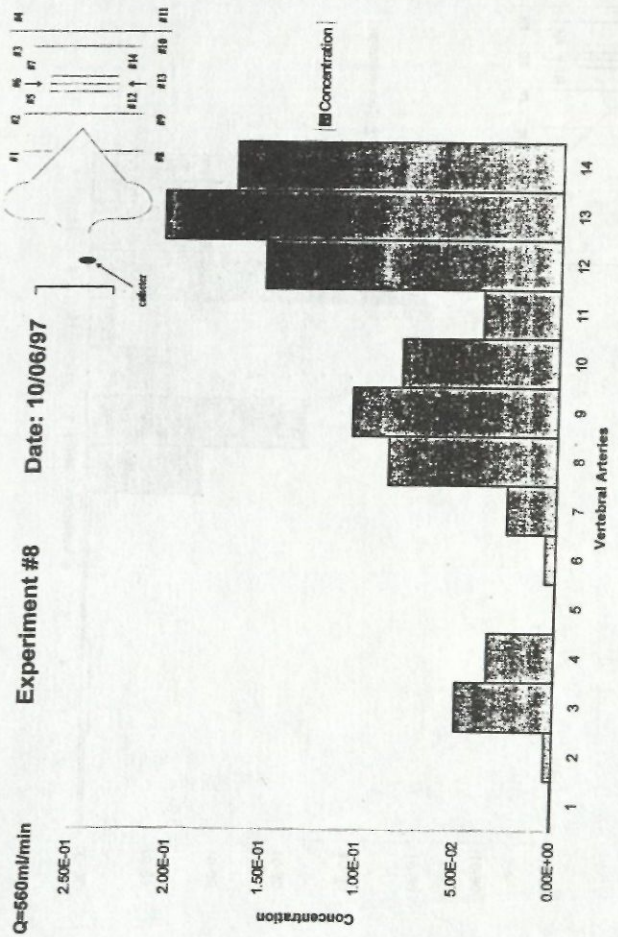

Figure 11. Results obtained from experiment 8

exp 9

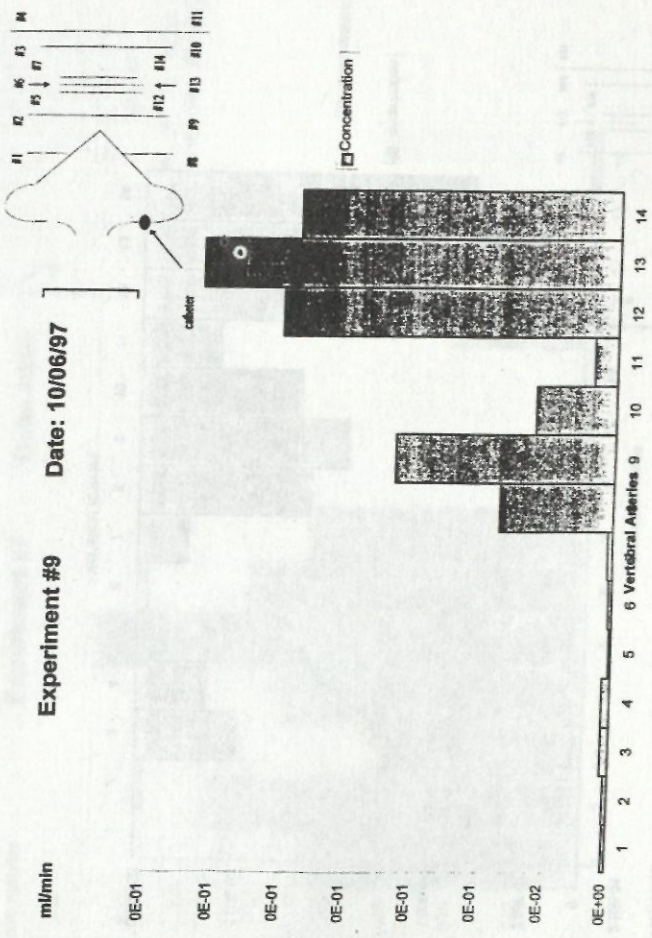

Figure 12. Results obtained from experiment 9

Finally, my supervisor suggested that we compare the data collected in the computer with the data collected by a Spectrophotometer to check if the results of both concentrations were proportional in the two different machines. They were. Figure 13 shows that the results are almost the same, but with different concentrations it is normal to have different numbers.

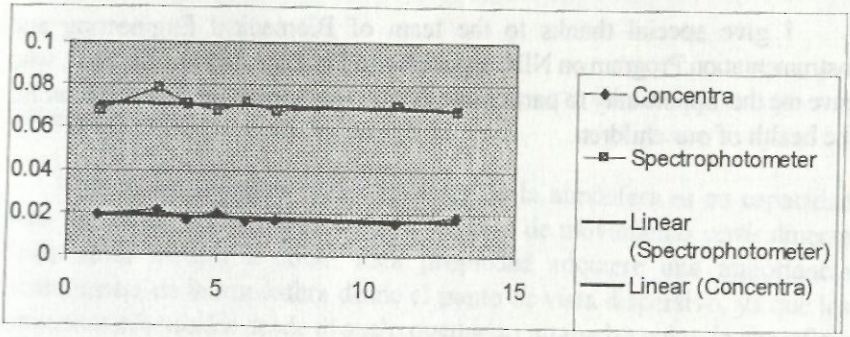

Figure 13. Comparison of concentra and spectrophotometer data vs a linear behavior

Conclusions

As I said before, we made these experiments to see whether it was viable to perform the physicians' experiments in human beings. However, we noticed that the glycerin velocity was too slow (Low Reynolds number) and that the fluid was laminar. For that reason the dye (representing the drug) did not mix well with the glycerin. There were not enough forces to break the kinematics forces of the glycerin. These forces created streams in the dye keeping the fluid from mixing well.

In these experiments we saw a proportional distribution in the right part of the model, especially when the catheter was inserted in the right vertebral artery and a proportional distribution in the left part of the model when the catheter was inserted in the left vertebral artery. This research determined that

these experiments are viable only if the drug is applied simultaneously in both both vertebral arteries. When we finished these experiments my supervisor invited the physicians to see the model. He explained them how it works and showed them the results. They became hopeful and got excited with the positive results and stated that, based on the results, they were going to start experimenting with animals. Afterwards, if they get positive results, they are going to start making experiments in children.

I give special thanks to the team of Biomedical Engineering and Instrumentation Program on NIH, especially to Dr. Lutz and Dr. Dedrick, who gave me the opportunity to participate during this important investigation for the health of our children.