Journal of Engineering Physics and Thermophysics, Vol. 69, No. 3, 1996

BIOFLUID MECHANICAL STUDIES IN MODELS OF BLOOD VESSELS AND SOME APPLICATIONS

D. Liepsch

UDC 612.13

Lasers are used in a wide variety of medical applications. While laser catheters have beem developed for highly accurate velocity measurement, these are invasive; noninvasive techniques are more desirable but not as precise. The laser is, however, a great tool for in vitro measurements. Several groups internationally are using the laser in the study of local velocity distribution in microscopic areas of specially constructed models. Laser Doppler anemometry is widely used to measure the local, time-dependent velocities, while phase Doppler anemometry has been developed to measure particle size, distribution and velocity. Most recently, laser analyzer techniques have been developed for analyzing the particle size of two phase flow systems. It has become increasingly important for physicians to visualize blood flow. In addition to the techniques mentioned above, several laser sheet techniques have been developed for precise measurements. This paper presents a short review of laser techniques and shows some applications especially for the laser-Doppler anemometer.

1. INTRODUCTION

Biofluid mechanics is a new field whose importance to the field of bioengineering has increased in importance over the last two decades. Important interdisciplinary research between engineers, biochemists, biophysicists, physicians, and electronic engineers is scarce; however the advantages of cooperation to achieve common goals are becoming increasingly obvious. As a beginning, a fundamental understanding of the flow behavior of all biological fluids – water, gas, blood, tissue fluids – in all living species including plants, is important. The movement and balance of forces in resting fluids and fluids in motion are subjects for research.

Biofluid mechanics is important for understanding blood circulation and microcirculation and how these affect: atherogenesis; respiratory systems; artificial organs, artificial grafts, heart valves and artificial vessel development; surgical techniques (end-to-end, end-to-side anastomosis) that may be affected by varying geometries; urological studies including artificial urethra development and use of sonic waves to destroy kidney stones; whole blood rheology; mass and material transport through membranes; wave propagation; and diffusion processes, development of pharmaceutical agent which affect blood and tissue.

Most studies in these important areas must first be carried out in models. Models have many advantages compared to *in vivo* measurements. For example, it is still not possible to localize small deposits and to measure the velocity profiles with a high local resolution using ultrasound or magnetic resonance imaging. These two promising methods are being improved by model measurements leading to further analysis of flow; e.g. if the flow goes backward or forward (alliance effect for colored ultrasound signals). A correlation between high local resolution laser Doppler anemometer techniques and MRI or ultrasound techniques will certainly enhance our understanding in the near future. A main goal for the future, therefore, is to develop noninvasive measuring techniques for use with patients.

The advantages of model studies is that the experiments are reproducible. With animal studies the parameters differ from species to species. A very important application of biofluid mechanics in models is atherosclerosis and aging. Fundamental studies can be done in models to analyze the influences of different flow

Institut für Biotechnik e.V. and Fachhochschule München, 34 Lothstr., München, 80 335, Germany. Published in Inzhenerno-Fizicheskii Zhurnal, Vol. 69, No. 3, pp. 399-412, May-June, 1996. Original article submitted March 20, 1996.

 1062-0125/96/6903-0316$15.00

parameters. These parameters are: steady-unsteady flow, elasticity of the wall, non-Newtonian flow behavior, shear stress on blood cells, interaction between cell/cell and cell/vessel wall, the change of the cell membrane under shear stress. It is also necessary to develop new biomaterials for such treatments as vessel surgery. New biomaterials and new technologies can be easily tested in models. Here the development of different laser techniques will help to solve several problems with *in vivo* and *in vitro* measurements.

This paper focuses on research in atherosclerosis in a human carotis bifurcation. Here, the engineer can study several fundamental flow reactions. It has been shown in relatively young men that small deposits are already formed directly downstream of bifurcations and bends in the arterial system. The risk factors for atherosclerosis are well known. These include hypertension, hyperlipidemia, diet (high fat, high cholesterol, obesity), smoking, stress, diabetes mellitus. Variables in the atheroscrelotic process are: fibrinogen level, red cell deformability, hematocrit, total cholesterol, low density lipoprotein (LDL) cholesterol, and plasma triglycerides. Factors that contribute to the genesis of atherosclerosis are: hemodynamic factors, architecture of the vasculature, properties of blood.

The influence of some biofluid mechanical factors in the circulatory system can be seen in the study described below. These studies were only possible with a high temporal and spatial resolution system, e.g., a laser Doppler anemometer (LDA). We started with simplified glass models to study the influence of the branch angles, tube diameter ratio at different flow rate ratios. Then we continued with elastic silicon rubber models. The influence of the elasticity could be demonstrated precisely. Finally non-Newtonian fluids similar to blood were studied in the models.

2. METHODS

2.1. Flow Visualization Using Lasers. Flow visualization is used to obtain an overall view of the flow behavior. Many flow visualization techniques exist in addition to laser. These include dyes, bubbles, birefringent solutions. A widely used flow visualization technique is the laser sheet technique. Of laser sheet methods, the so-called particle image velocimetry is most common. Here a laser beam creates a laser sheet using a cylindrical lens. With this technique a very thin light sheet of about 0.2 mm can be created. When seeding particles are added to the fluid, the movement of the particles in the illuminated field can be observed. The added particles should follow the flow completely. Particle movement can be fixed by a series of photographs or, better, by video. The images can be analyzed using fast Fourier transform, cross- or auto-correlation techniques.

With digital particle imaging velocimetry, the images are recorded using a video camera, the pictures are processed using a digital image processing system. Several images are selected and digitalized. The displacement of particles is calculated using a cross correlation of the images. Another method is Young's fringe technique in which several images of the particle field are imposed at successive times on a photographic record. The negative is analyzed on an optical bench using a laser to scan the negative over its surface. In the illuminated area the particles produce scattered patterns, which corresponds to the 2D Fourier transform. Each particle will produce a coherent scattered pattern similar to Young's fringes. The direction of these fringes is perpendicular to the motion of the particles and the space is inversely proportional to the distance between the images and to the local velocity. The fringe pattern can be analyzed with a digital imaging processing system to determine the fringe direction and fringe spacing. Having the entire negative scanned, the whole flow field can be obtained. In addition to the He-Ne or Argon laser, pulsed laser light sources can be used [1].

An elegant method uses photochromic dye and a pulsed laser. An optical arrangement splits and focuses the UV beam producing simultaneous dye traces in the photochromic solution, e.g., Trimethyindoline nitrobenzospiropyran. The traces are produced in a very short time following the laser pulse (<1 μsec). The trace displacement particle are then photographed at a fixed delay with a flash. A microcomputer controller is used to trigger the flash, camera and laser. With this method, studies can also easily be done under pulsatile flow conditions. The velocity profiles can be easily observed [2].

2.2. Laser-Doppler-Anemometry. Unlike the laser flow meter, which measures blood flow in capillaries, the laser cannot be used normally in *in vivo* velocity measurements, because the laser light is absorbed by the red cells.

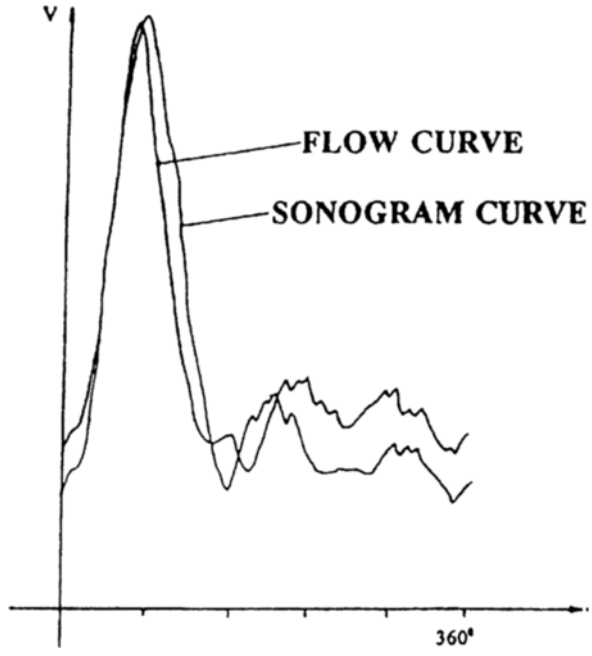

Fig. 1. Flow curve in the common carotis of a healthy person recorded with a pulsed ultrasound compared to the flow curve created by a piston pump from the model experiment.

Another important factor is that the blood vessels would have to be transparent so that the laser could go through. The laser-Doppler-anemometer is therefore used in model studies.

The principle of the LDA has already been described several times [3, 4]. A laser beam is divided into two beams and a focus point is formed over Bragg cells and a lens. This is the so-called measuring point, consisting of an ellipsoid. The measuring point in commercial systems normally has a dimater of ~100 μm (length of the diameter of the axis). We have constructed LDA systems with a spatial resolution up to 20 μm. This depends on the beam distance and the focus length of the optical lens. Japanese scientists have also developed a laser-Doppler-anemometer microscope with a resolution of 10 μm.

LDA has several advantages: it does not disturb the flow, has a high spatial resolution up to 10^{-4} mm^3 (in our system we worked with a sample volume of about $5 \cdot 10^{-4}$ mm^3), and has a fast response. We used a 5 mW He-Ne laser and also 2 W Argon laser in a forward and backward scattered light system. The Doppler frequency real-time demonstrator used for LDA measurements was a tracker, which locked on to the Doppler frequency and tracked the instantaneous frequency as long as the internal servo loop stayed locked. The dynamic range of trackers limits the tracking ability to about 30% rms frequency fluctuations in the measuring range of 15 MHz. We also have used counters and a burst spectrum analyzer for some measurements. The data were stored using an AID converter on a hard disc and also observed and recorded with an oscilloscope.

The experimental flow system for the velocity measurements has also been described several times [5, 6]. Our model was mounted in an X-Y-Z table equipped with a stepping motor. By moving the table perpendicularly to the tube axis, the velocity profile over the entire tube diameter was recorded for steady flow. For unsteady flow we used a piston pump and superimposed a pulse wave over the steady flow (Fig. 1). The curve was similar to flow curve measured with an ultrasound. The pulsatile LDA measurements were done at 9 measuring points over one diameter, step by step [7]. We divided one cross section into nine diameters and measured the velocity over these nine diameters. The stored velocities were plotted as a three dimensional graphic using a computer program.

The fluid is pumped from a receiver into a reservoir. Nitrogen or compressed air is used instead of a pump for non-Newtonian fluids to avoid destroying the long chain molecules. From the reservoir the fluid flows into an overflow container, which creates a constant static pressure in the model. The volume flow and volume flow rate ratio is adjusted by using small, highly variable regulator tanks and by weighing the fluid. The fluids used were a

glycerine water solution with a dynamic viscosity η = 9.11 MPas and a density of ρ = 1147 kg/m^3 to match the refraction index of the silicon rubber wall of the model. The non-Newtonian fluid was a 51.7% aqueous Dimethylsulfoxide solution mixed 1:1 with a mixture of 0.000% AP45 and 0.007% AP302 aqueous polyacrylamide solution. This fluid has the same total viscosity as human blood in a shear rate range from 8–200 1/sec. It shows a shear thinning and thixotropic behavior at low shear rates. The whole model was embedded in a glycerine water solution, so that the laser beams would pass the model without any refraction.

We used an elastic silicon rubber model of a carotis artery prepared from a healthy human accident victim. The model technique has been described several times. Our models have an elasticity similar to the vessel wall. In addition to this model, we also used a model with a 90% stenosis in the internal carotis.

RESULTS

Figure 2 shows the velocity profiles in the common carotis 15 mm upstream of the branching point into the externa and interna carotis. The average Reynolds number for the whole pulse cycle was Re = 250. The average velocity was calculated from the flow over a whole pulse cycle divided by the cross section of the common carotis. The phases 0°, 34°, 67°, 90°, 120°, and 175° were always recorded. The Wormersley parameter

$$\alpha = \mathrm{Re}\sqrt{\omega/\nu} = 3.0$$

where R is the radius of the artery, ω the random velocity and ν the kinematic viscosity. The fluid was a glycerine water solution. The scale shows the local velocity to the average velocity over the whole cross section. Fully developed laminar profiles can be seen. By comparison, with the non-Newtonian fluid (Fig. 3) the velocity profiles are flattened. Figure 4 shows the velocity profiles at different phase angles 2.5 mm downstream of the branching point. The flow rate ratio of the interna carotis Q_2 to the carotis communis Q_1 was 0.7. That means 70% of the fluid flows into the interna carotis. A small flow separation region can be seen at the outer wall (OW1) especially at the phase angles ωT 67° and 90°. This experiment was repeated with non-Newtonian fluid (Fig. 5). No direct flow separation region is seen at the outer wall, however at ωT 90° and 120° in the center, the velocity is almost zero.

Figure 6 shows the velocity profiles for the externa carotis 2.5 mm downstream of the branching point. No flow separation exists, whereas with the non-Newtonian fluid at ωt = 120° a small reverse flow is observed (Fig. 7).

Finally in Fig. 8, the velocity profiles in a 90% stenosed model are shown for the non-Newtonian fluid. The jet effect can be observed clearly. High shear rates exist. The profiles are very flat in the stenosis as expected. Further downstream we can observe a very highly disturbed flow with reverse flow areas (Fig. 9).

3.1. Phase Doppler Particle Analyzer and Laser Particle Sizer. We also studied different two phase flow systems using a phase-Doppler particle analyzer and a laser particle sizer from Fritsch Co. These studies were done in a 90°-T-junction. We added biconcave, disc-shaped particles with an average diameter of 6 μm in a concentration of 1% in a 40% aqueous glycerol solution. We also tested ghost cells up to a concentration of 40%.

The phase Doppler particle analyzer gave good results. The velocity frequency of the particles passing through the laser beam intersection region gives the velocity component perpendicular to the interference grid. The phase shift is inversely proportional to the particle diameter. We also analyzed the solution with a laser particle sizer, in which the laser light is scattered at the particles in a measuring cell. A special detector measures the angle and intensity curve.

CONCLUSION

With the different laser systems very precise measurements are possible. With the LDA system details of Newtonian versus non-Newtonian fluids and the movement of the wall can be studied. The LDA system and the phase Doppler Analyzer allow precise two-phase flow measurements in models.

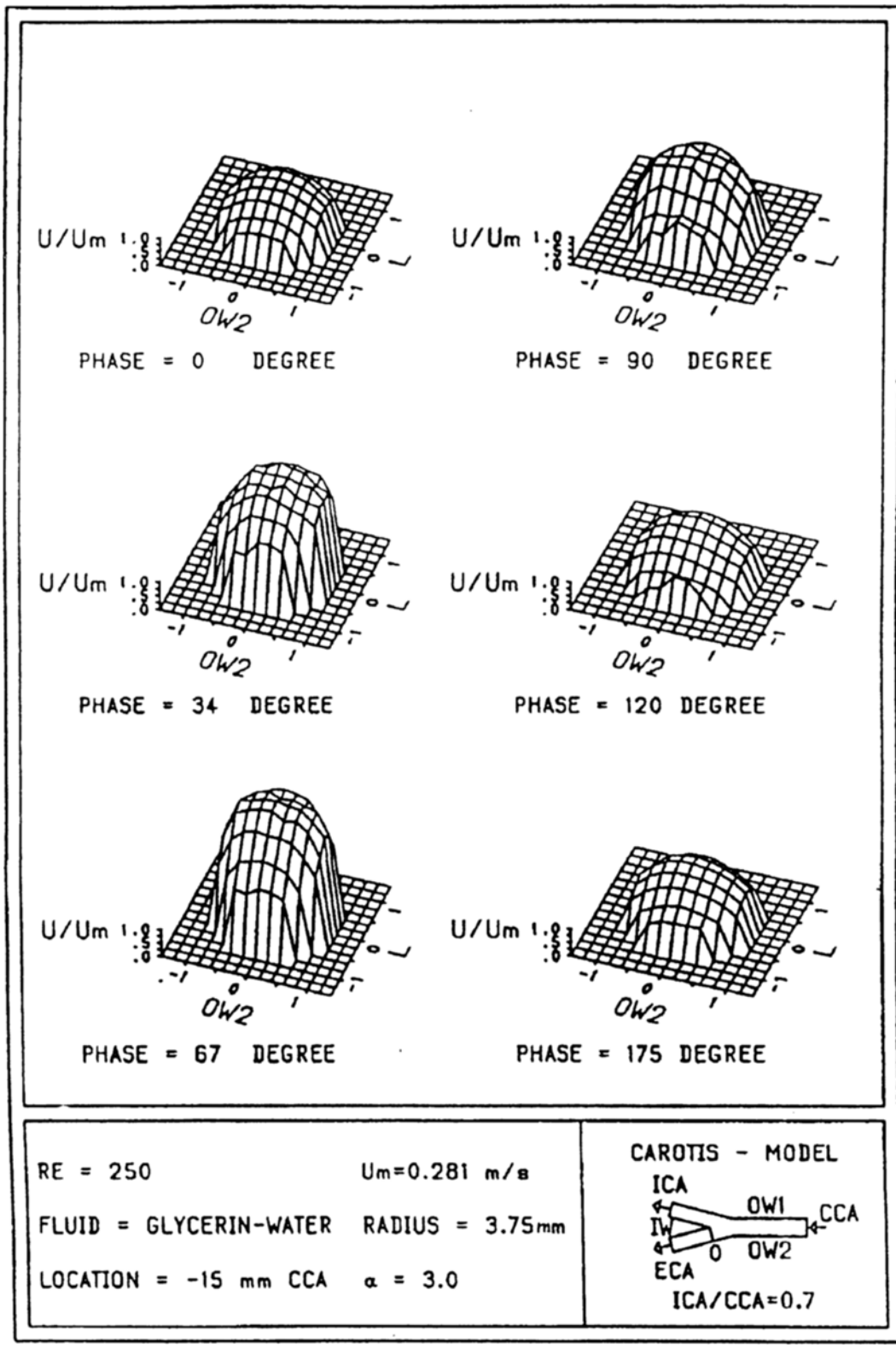

Fig. 2. Velocity profiles over a whole pulse cycle (phase $\omega T = 0^{\circ}$, 34°, 67°, 90°, 120°, 175°) recorded with an LDA in the common carotis at a Womersley parameter $\alpha = 30$ and an average Reynolds number over the whole cross section of Re = 250 15 mm upstream of the bifurcation point. The fluid used is a Newtonian glycerine water solution.

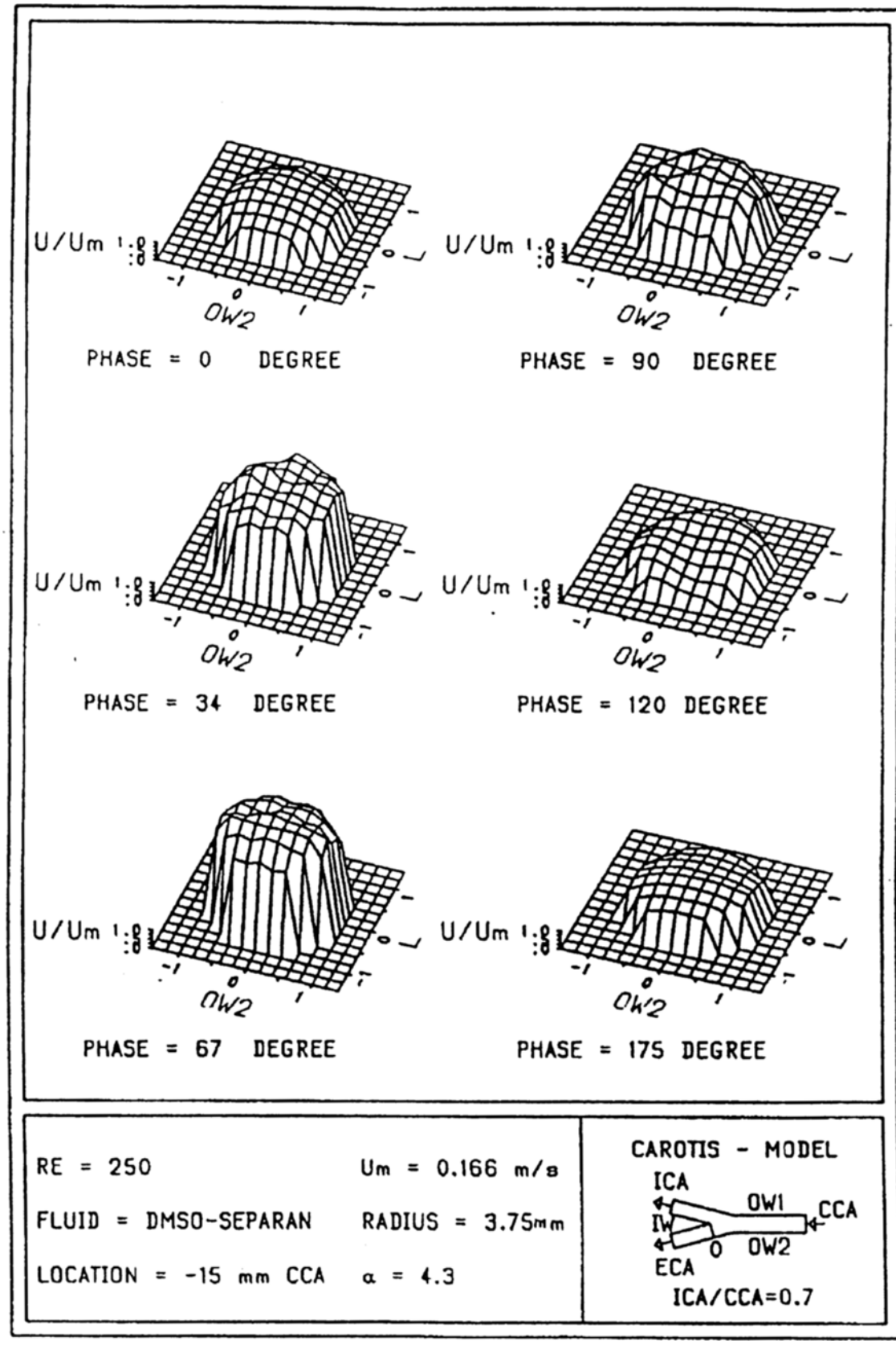

Fig. 3. The same velocity measurements as in Fig. 2 but with a blood-like non-Newtonian fluid.

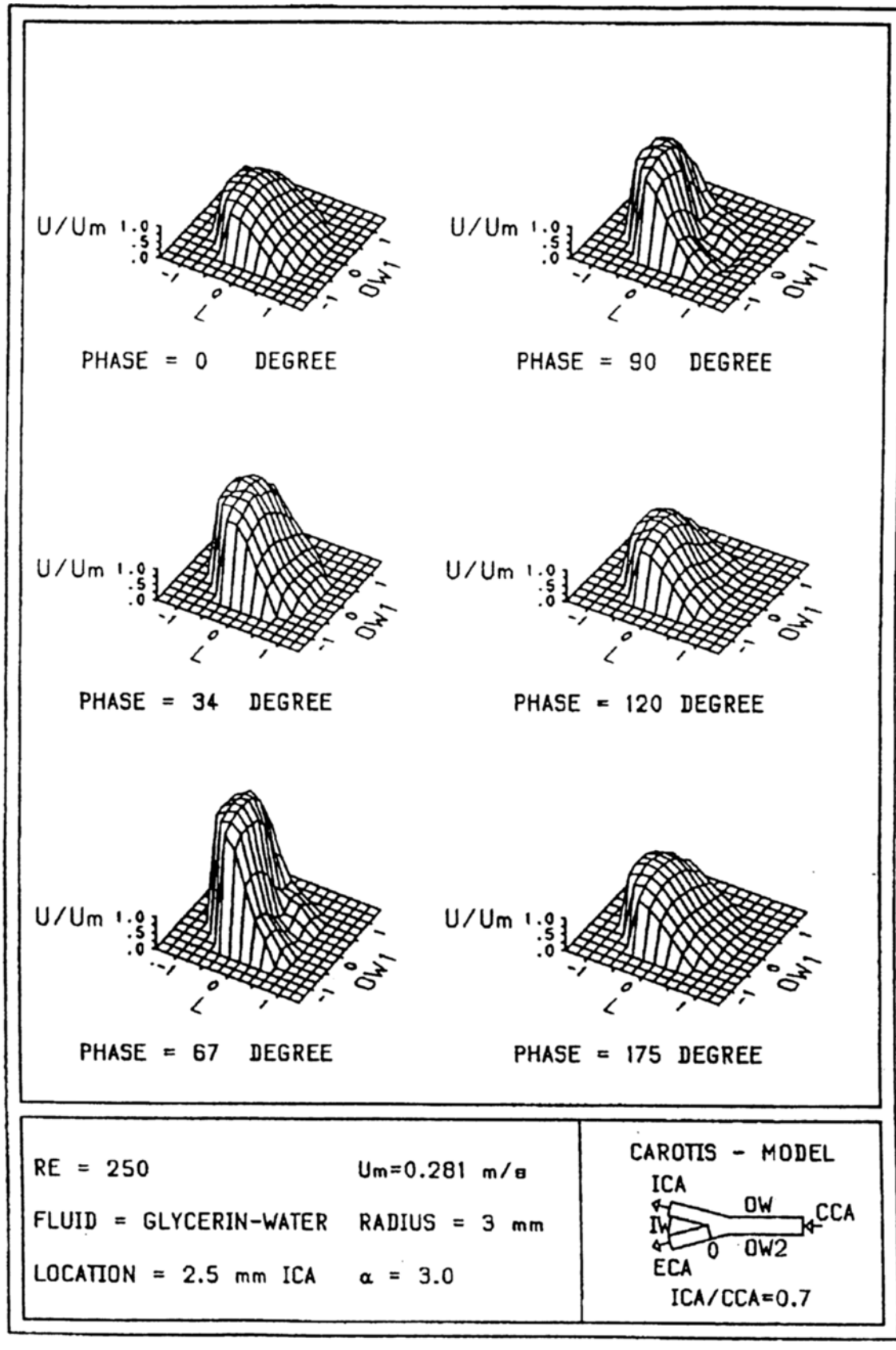

Fig. 4. Velocity profiles over the whole pulse cycle for a Newtonian glycerine water solution 2.5 mm downstream in the interna carotis. Re = 250.

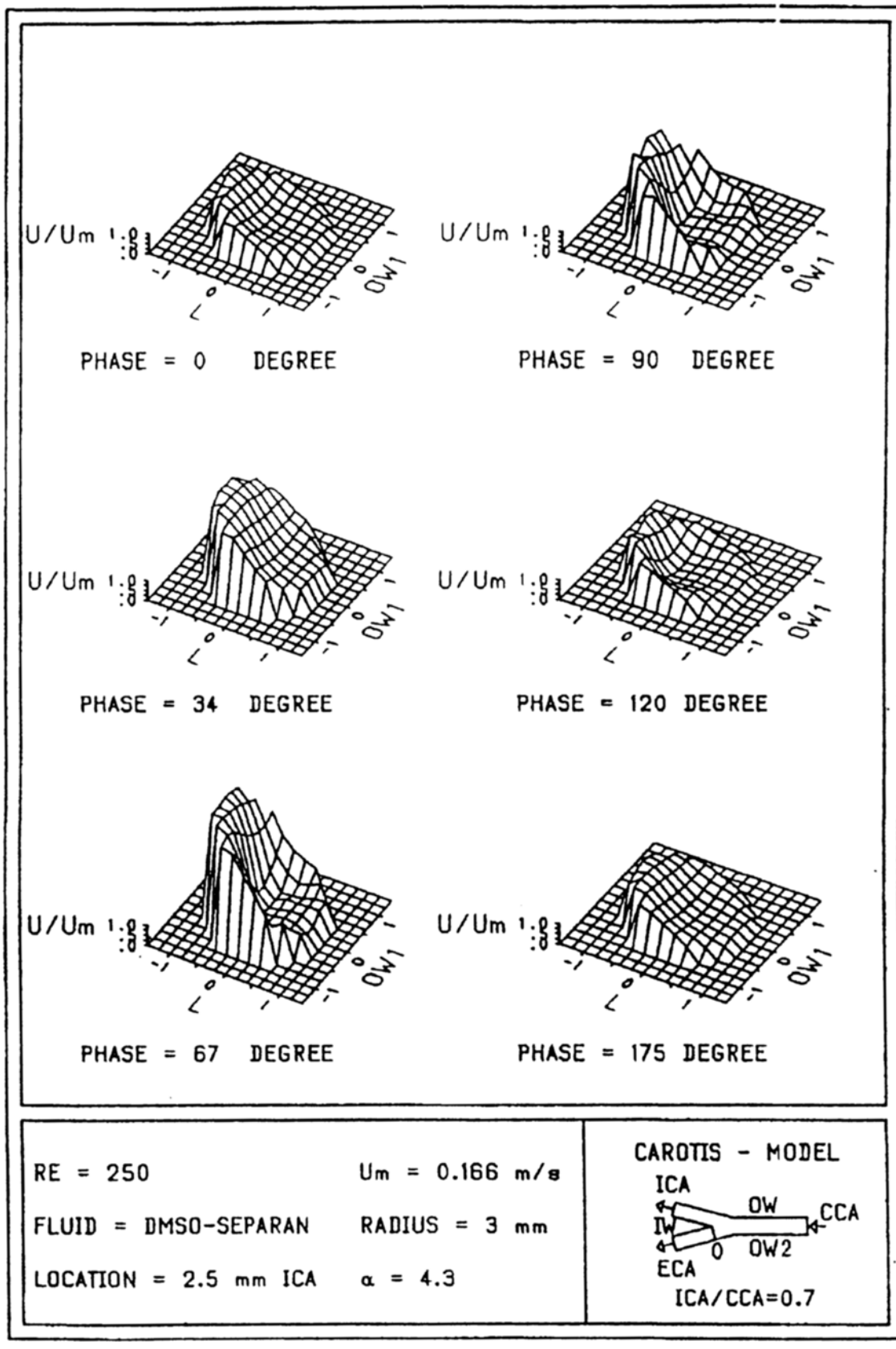

Fig. 5. The same measuring points as in Fig. 4 with a non-Newtonian blood-like fluid.

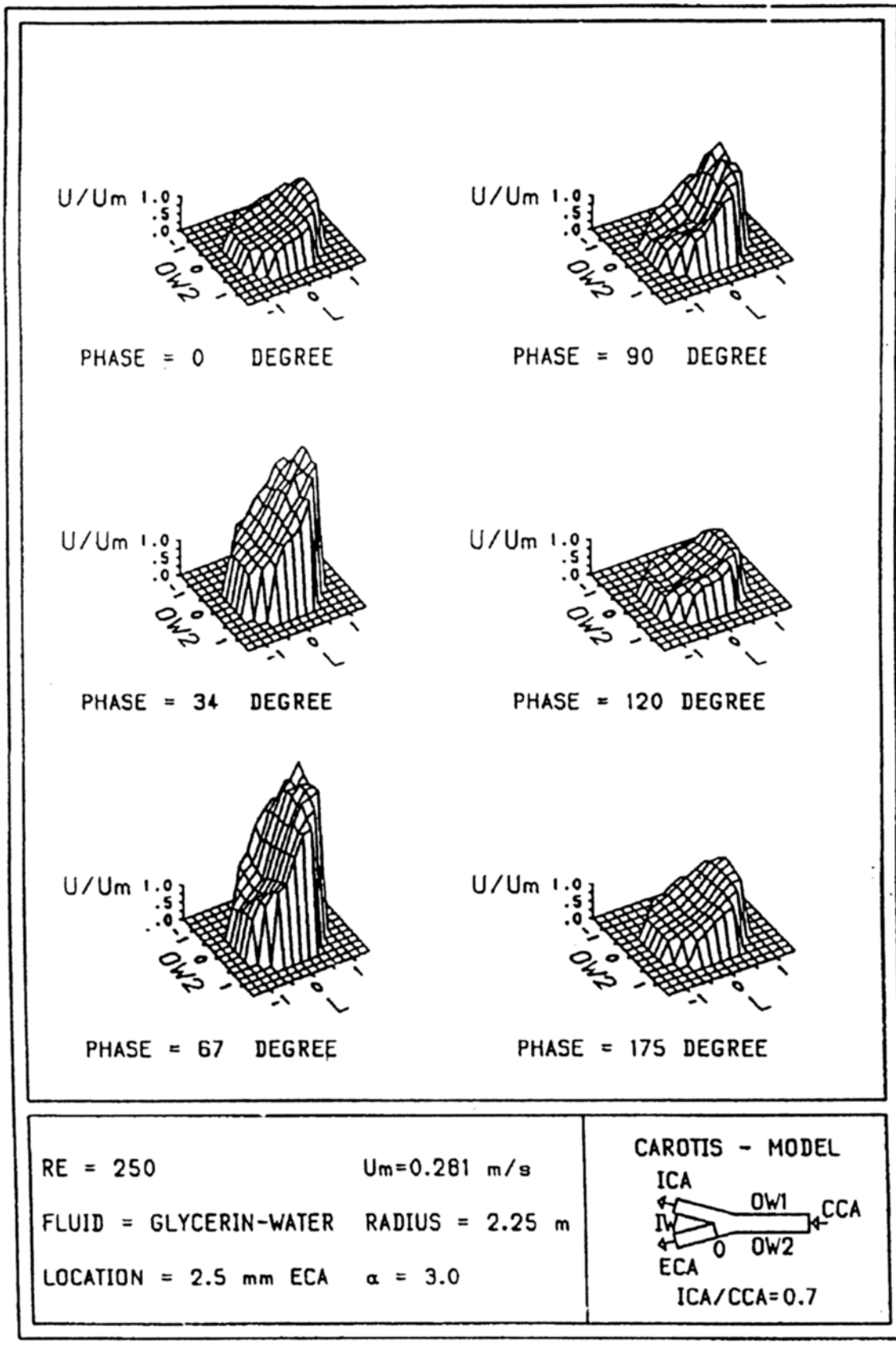

Fig. 6. Velocity distribution 2.5 mm downstream in the externa carotis using a glycerine water solution.

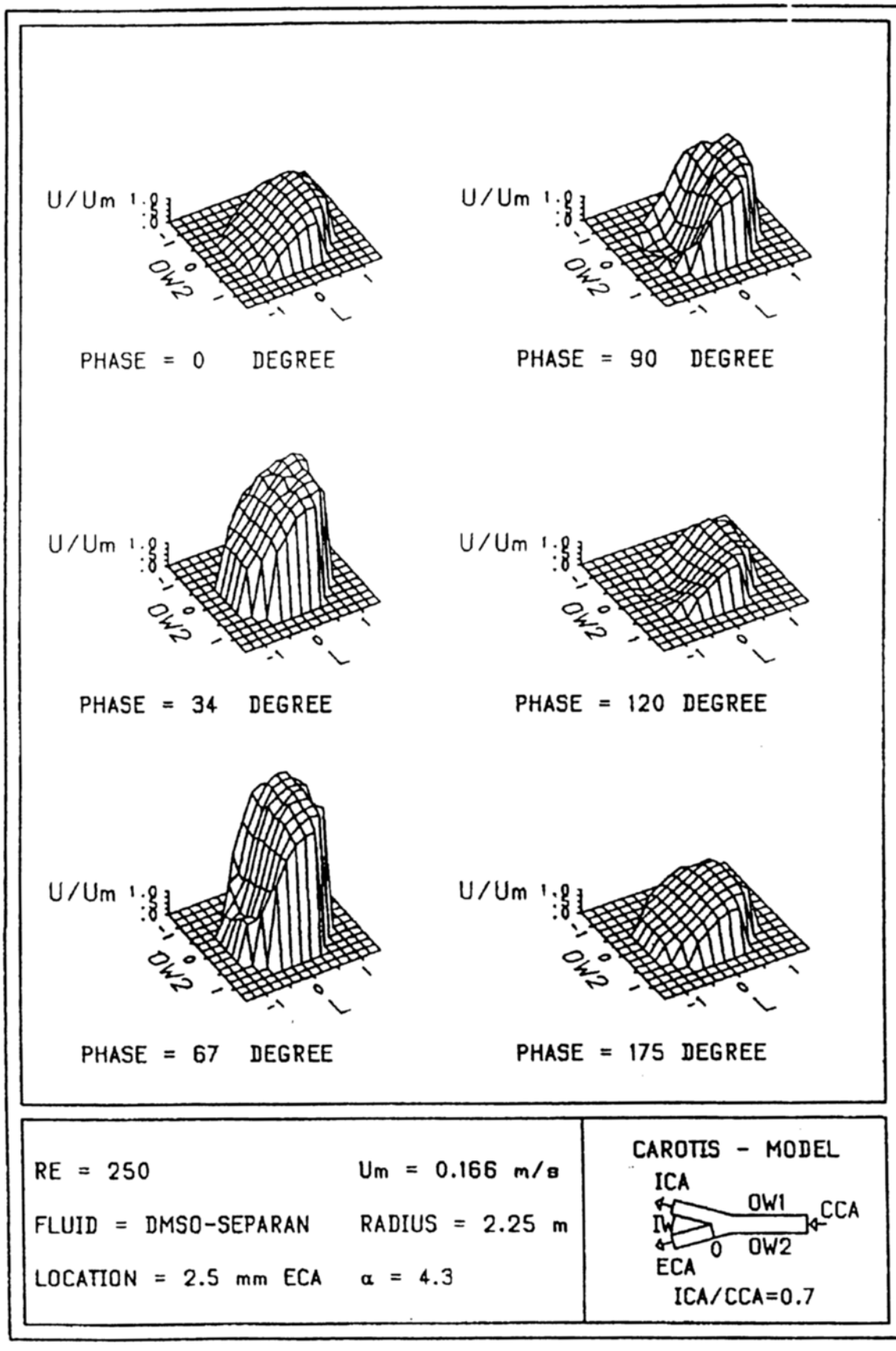

Fig. 7. The same measuring points as in Fig. 6 for a non-Newtonian fluid.

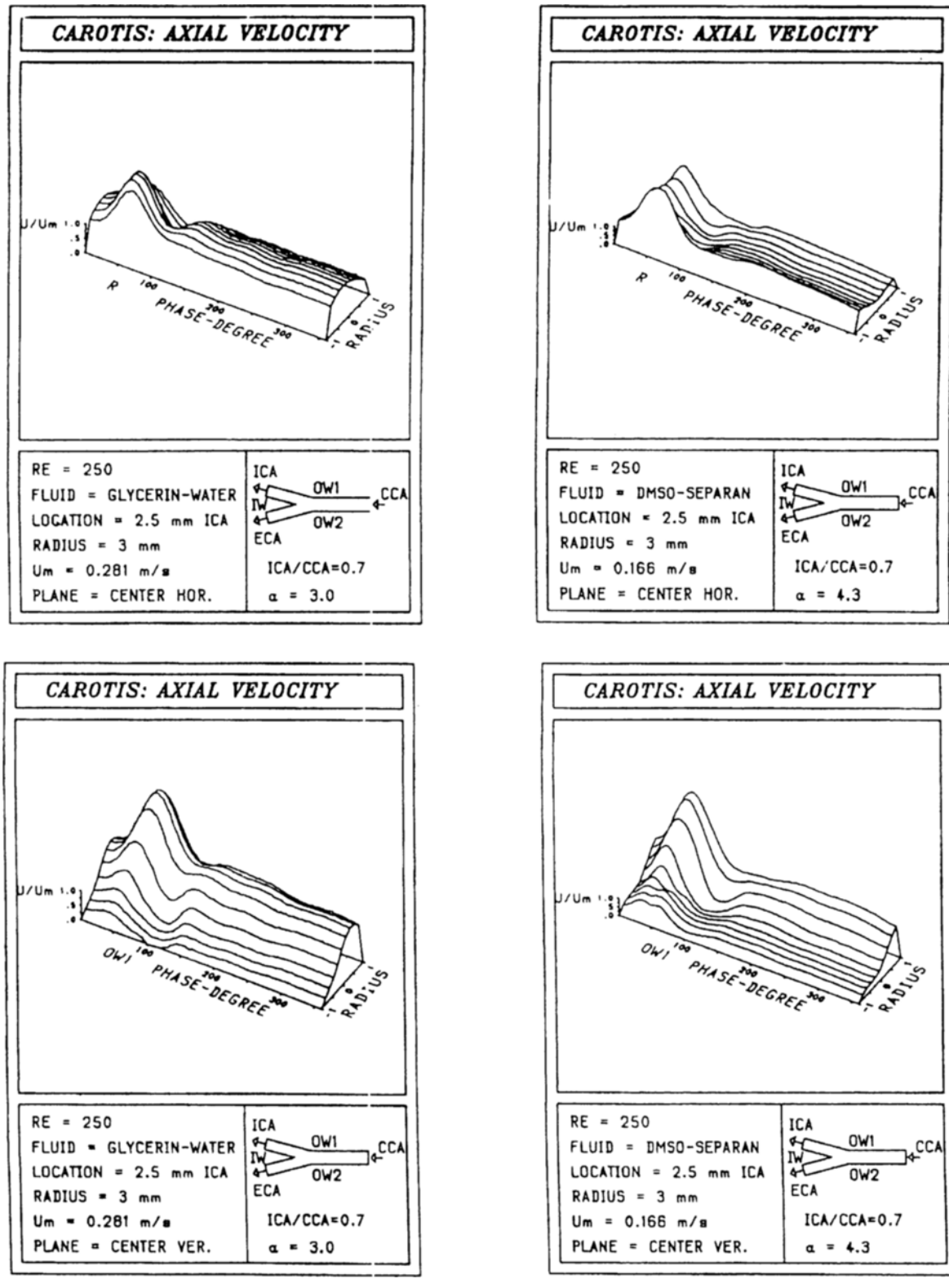

Fig. 8. Axial velocity distributions for mixture glycerin–water (a), DMSO–separan (b), glycerin–water (c), DMSO–separan (d).

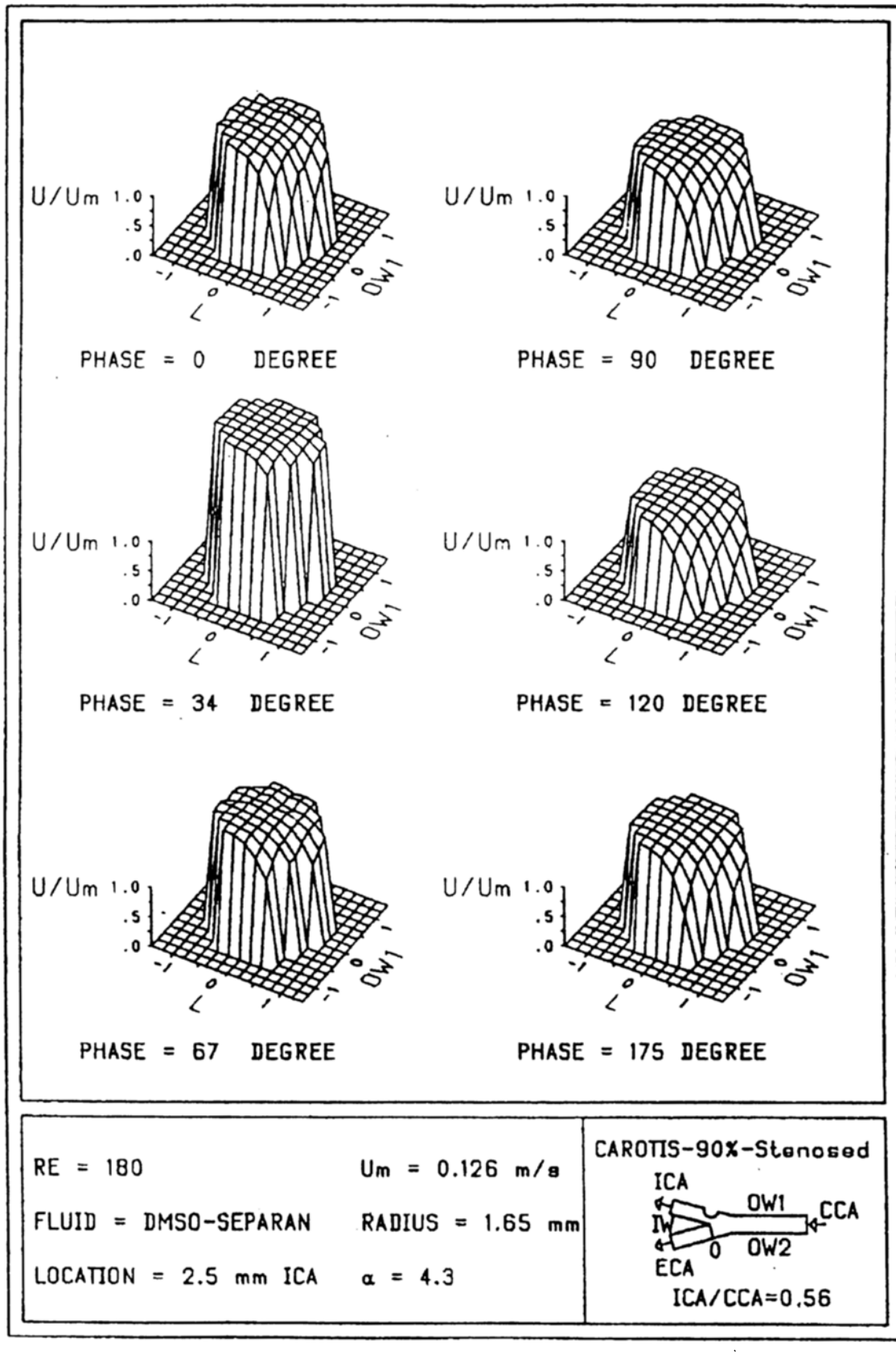

Fig. 9. Velocity distribution 2.5 mm downstream in the interna carotis with a 90% stenosis.

Laser velocity measurements in models can be used to support ultrasound and MRI measurements *in vivo*. A correlation between these three methods in models will lead to a more accurate interpretation of the ultrasound and NRI signals when used in patients.

REFERENCES

1. P. Corieri and M. L. Riethmudotdotkker, A comparison between laser techniques used to analyze velocity fields in biological bifurcation models. In preparation.
2. M. Ohja, S. C. Cobbold, K. W. Johnston, and E. R. Ethier, in: Proceedings of the 2nd International Symposium on Biofluid Mechanics (ed. by D. Liepsch), Springer Verlag, Heidelberg Berlin (1990).
3. F. Durst, A. Melling, and J. H. Whitelaw, Principle and Practice of Laser-Doppler Anemometry, Academic Press, London (1976).
4. D. Liepsch, Untersuchungen der Strömungsverhältnisse in Verzweigungen von Rohren kleiner Durchmesser (Koronararterien) bei Stromtrennung, VDI Berichte, 232, 423-442 (1975) und Diss. TU Mudotdotnchen (1974).
5. D. Liepsch, Strömungsuntersuchungen an Modellen menschlicher Blutgefäßsysteme, VDI-Forstschrittberichte Reihe 7: Strömungstechnik Nr. 113, VDI Verlag, Düsseldorf (1987).
6. D. Liepsch, A new three-dimensional laser Doppler anemometer, in: Advances in Bioengineering, BED, 8 (ed. By G. R. Mudotdotller) (1988), pp. 3-6.
7. St. Moravec and D. Liepsch, Flow investigation in a model of a three-dimensional human artery with Newtonian and non-Newtonian fluids, Biorheology, 20, 745-759 (1983).