Project # E-25-635   MOD # _____   REV # 0__
Contract # MSM-8704973_____   OCA file # ___   Status A
Contract entity   GTRC   Prime contract # _____
PDPI VITO R P_____   (DR.
    SSN   - -   Unit $M E$ Phone (   ) 4 - 2792
Project unit ME_____   Unit code 02.010.126
 Sponsor/Division NATL SCIENCE FOUNDATION__ / GENERAL_____
 Sponsor#/division #   107 / 000
 Type of document   GRANT__
 Award period: from 87 / 06 / 15 to 88 / 11 / 30 (perf) 89 / 02 / 28 (rpts)
Sponsor amount   New this change   Total to date
    Contract value $ _____42357   _____42357
    Funded $ _____42357   _____42357
 Cost sharing # _____   Cost sharing $ _____42358
 Does subcontracting plan apply? (Y/N) N
 Title -
EQUIPMENT FOR BIOMECHANICS RESEARCH: AN IMAGING SYSTEM_____

CTR project # R6334-0A0_____   CTR cost sharing # _____

Are there existing subprojects? (Y/N) N
Is this a subproject? (Y/N) N   Main project # _____
Continuation of project # _____   Type of research   RES____

Coproject director name
    GIDDENS D P_____   (DR.
    SSN 256-50-6038   Unit AE

Coproject director name

    SSN   - -   Unit

PROJECT ADMINISTRATION DATA

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Security class (U,C,S,TS) U_   ONR resident rep. is ACO (Y/N) N
Defense priority rating _____
NSF___ supplemental sheet
Equipment title vests with Sponsor _   GIT X   Comment follows -

Admin comments -
PROJECT INITIATION_____

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

SR-147

Closeout Notice Date 04/24/90

Project No. E-25-635_____   Center No. R6334-0A0_____

Project Director VITO R P_____   School/Lab MECH ENGR_____

Sponsor NATL SCIENCE FOUNDATION/GENERAL_____

Contract/Grant No. MSM-8704973_____   Contract Entity GTRC

Prime Contract No. _____

Title EQUIPMENT FOR BIOMECHANICS RESEARCH: AN IMAGING SYSTEM_____

Effective Completion Date 881130 (Performance) 890228 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	N	_____
Final Report of Inventions and/or Subcontracts	Y	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

Comments_____

Subproject Under Main Project No. _____

Continues Project No. _____

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	N
GTRC	N
Project File	Y
Other _____	N
_____	N

NOTE: Final Patent Questionnaire sent to PDPI.

6-APR-90

TO WHOM IT MAY CONCERN:

I am submitting the attached final report for NSF award #MSM 8704973 entitled <u>Equipment for Biomechanics Research: an Imaging System</u> R.P. Vito principal investigator and D. Giddens, co-investigator. The equipment purchased, a high speed imaging system, has been in use for some time now. It is being used extensively in two funded projects:
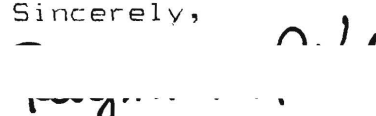
> <u>Hemodynamic Determinants of Regional Vulnerability: Near Wall Flow Phenomenon and Particle Dynamics</u> D.P. Giddens, Principal Investigator, R.P. Vito, Faculty Associate, NIH SCOR

> <u>Vascular Healing: Cell Rheological Factors</u> D.P. Giddens, Principal Investigator, R.P. Vito, Faculty Associate, NIH.

Both grants are large five year projects conducted in collaboration with the University of Chicago. A number of investigators are involved at each Institution.

The support of Biomechanics research in Mechanical Engineering by the National Science Foundation and the Georgia Institute of Technology is greatly appreciated.

Sincerely,

Raymond P. Vito
Associate Professor

NATIONAL SCIENCE FOUNDATION Washington, D.C. 20550	**FINAL PROJECT REPORT** NSF FORM 98A

PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING

PART I—PROJECT IDENTIFICATION INFORMATION

1. Institution and Address Georgia Institute of Technology Atlanta, Georgia 30332-0405	2. NSF Program Research Equip. NSF 84-51	3. NSF Award Number MSM 8704973
	4. Award Period From **6-87** To **12-88**	5. Cumulative Award Amount 42,357

6. Project Title

"Equipment for Biomechanis Research—An Imaging System"

PART II—SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

The purpose of this project was to purchase a major piece of scientific equipment for use in bioengineering research. The equipment purchased is a high speed video camera and recorder system. The system can be used to record video images of high speed motions. Examples include soft tissue deformations as related to tissue injury and the movement of particles in a flowing fluid as related to the development of atherosclerosis. The equipment is in use in several research projects related to patency of vascular grafts, deformations of the human cornea and study of physiological flows. It is also currently used in two non-bioengineering studies related to movement of paper through a processing machine and a tribology application.

PART III—TECHNICAL INFORMATION *(FOR PROGRAM MANAGEMENT USES)*

1. ITEM *(Check appropriate blocks)*	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (✓)	Approx. Date
a. Abstracts of Theses		X			
b. Publication Citations		X			
c. Data on Scientific Collaborators		X			
d. Information on Inventions	X				
e. Technical Description of Project and Results		X			
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)* Raymond P. Vito, PhD	3. Principal Investigator/Project Director Signature	4. Date 4/5/90

NSF Form 98A (1-87) Supersedes All Previous Editions

Form Approved OMB No. 3145-0058

PART III TECHNICAL INFORMATION

1a. Abstracts of Thesis

Attached.

1b. Publication Citations

Vito, R.P., Choi, H.S., Seifferth, T.A., Zarins, C.K., Glagov, S. and Bassiouny, H.S. Measurement of Strain in Soft Biological Tissues (invited paper) Developments in Theoretical and Applied Mechanics Proceedings of S.E. Conf. on Theor. and Appl. Mech. (1990)

1c. Data on Scientific Collagorators
Note: the Ph.D. students below are using the equipment in their thesis.

Don P. Giddens, Professor, Mechanical Engineering
Steve Dickerson, Professor, Mechanical Engineering
Ward Winer, Professor, Mechanical Engineering
Todd Seifferth, Graduate Student (M.S.)
Tom Shin, Graduate Student (Ph.D.)
Dung Chung, Graduate Student, (Ph.D.)
Yoon Su Nam, Graduate Student, (Ph.D.)
Tong Dar Tang, Graduate Student, (Ph.D.)
Raychang Tsao, Graduate Student, (Ph.D.)
Steve Jones Ph.D., Research Engineer

1d. Information on Inventions

No inventions resulted from this study.

1e. Technical Description of Project and Results

The purpose of this project was to purchase a major piece of scientific equipment for use in bioengineering research. The equipment purchased is a high speed video camera and recorder system. The system can be used to record video images of high speed motions. The equipment is being used both for measuring strains in soft biological tissues and for quantitative flow visualization. Both application involve frame by frame tracking of particles. Particle position information is then used to determine strains and velocities.

Specific applications include the measurement of strains in the region of an end-to-side anastomosis (abstract enclosed), and quantitative flow visualization in models of physiological flows pertinent to the study of the initiation and proliferation of arterial disease.

Additional studies in the areas of controls (machine handling of paper) and lubrication (hot spots in dry friction).

by

Todd Seiffereth

SUMMARY

Arterial disease has been established as a contributing factor in 50% of the total deaths in the United States. Arteriosclerosis, the most common arterial disease, frequently develops in peripheral limbs, restricting blood flow, creating pain, and jeopardizing limb viability. An artery bypass is often performed to correct the blood flow restriction by creating an anastomosis from a location proximal to the blood flow restriction to a location distal to the restriction. Upon completion of the artery bypass, normal blood flow is restored. However, for small diameter grafts, as required in peripheral bypass surgery, graft failure is a common occurrence. In biomechanics, a correlation between graft failure and soft tissue mechanical properties has been explored. It is hypothesized by others that the poor patency of small diameter vascular grafts is due in part to the mismatch of compliance between the host artery and the graft material.

The compliance mismatch in the region of a femoropopliteal end-to-side anastomosis, which is often the point of post-bypass failure, has not been studied due to its complex geometry. It is our hypothesis that the complex geometry of an end-to-side anastomosis may result in non-physiological strains in the bypass region. These non-physiological strains may lead to increased graft failure.

To help evaluate this hypothesis an *in-vivo* canine study was performed, in conjunction with the University of Chicago. The primary purpose of this study was to develop and evaluate an *in-vivo* method for measuring strains in the arterial wall and graft material as seen in the complex geometry of a small diameter end-to-side anastomosis.

Iliac-femoral bypasses were performed on both legs of four canine test subjects. A segment of saphenous vein was used for the right leg bypass, while a PTFE material graft was used for the left leg bypass. The method of particle

tracking was used for strain analysis. Small particles were placed on the artery wall and graft material at eleven specific test site locations for each leg of each test subject. Tape recordings of the test site locations were performed using an Ektapro 1000 high speed video imager system. Particle displacement, as a function of the cardiac cycle (time), were evaluated by manually tracking particle locations from the video tape recordings. Particle location and displacement data were fit to a linear polynomial equation for each time "t". Strain information follows directly from the derivation of these polynomial equations. By correcting for artery orientation with respect to the camera (x,y) coordinate system, strains in the axial and circumferential direction, e_{aa} and e_{cc} were calculated.

Data reduction on the strain history information was performed to eliminate the inconsequential effects of time. Two methods of data reduction were performed, average value analysis and Fourier harmonic analysis. Average value analysis was performed by simply taking the average of 30 points (approximately 2 cardiac cycles) of the strain history data. The Fourier harmonic analysis involved performing a fourier transform on the 30 points of data and computing the strain amplitude from resulting power spectrum. Each method reduced each strain history for each test site location to one piece of data.

The effects of the pressure differences between the left and right leg bypasses were eliminated by normalizing the post-bypass strain data by data from a pre-bypass test site. Normalized data was used to compare left leg strain to right leg strain at any specific site location. The effects of the pressure differences between left leg and right leg were assumed random for the statistical analysis evaluation since all eight legs were evaluated at one time. Thus, un-normalized data was used for statistical analysis.

Strain vs. axial artery position was evaluated for the circumferential strain, e_{cc}, the axial stain, e_{aa}, the maximum shear strain, γ_{max}, and the area dilatation, Φ' for both data reduction methods. Statistical analysis was performed on the reduced data using a statistical analysis of variance method.

Results of the statistical analysis were evaluated at three confidence interval, 95% (p=.05), 85% (p=.15), and 75% (p=.25). Whereas the 95% confidence interval shows significant differences between data sets evaluated, the 85% confidence interval can be said to show significant differences with less confidence, and the 75% confidence interval can be said to show probable differences. Significant differences were found between the right leg bypass (saphenous vein) and the left leg bypass (PTFE) for the γ_{max}, and Φ' strain values (p=.05, average value data). Significant differences with less confidence were found between the right leg bypass (saphenous vein) and the left leg bypass (PTFE) for the e_{aa}, γ_{max}, and Φ' strain values (p=.15, average value data and Fourier harmonic data).

Probable differences were found to exist across the suture line between a test site on the graft material and test sites in the anastomosis region for e_{aa} and Φ' (p=.25). Probable differences where also found for e_{aa} and Φ' between pre-bypass site #1 and post-bypass site #1 (p=.25). Probable differences were found for Φ' between test sites in the anastomosis region and those proximal and distal to the anastomosis (p=.25). It is concluded that the bypass graft affects the axial strain and area dilatation (75% confidence) by creating strain differences in the vicinity of the anastomosis and across the suture line (sites #1, #2, and #6), and by creating differences before and after the arterial bypass (site #1). Further, the difference in the graft material used between the left side bypass and the right side bypass creates affects the axial strain, maximum shear strain, and area dilatation in the artery wall.

MEASUREMENT OF STRAIN IN SOFT BIOLOGICAL TISSUES

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ABSTRACT

This paper describes the application of particle tracking to the measurement of strains in soft tissues under **in-vitro** and **in-vivo** conditions. The methodology is outlined and application to two problems is discussed. Specifically, the biaxial mechanical testing of the pericardium and the measurement of strains in the vicinity of an anastomosis.

INTRODUCTION

In biomechanics, it is important to know how soft tissues react to mechanical loading under both **in-vivo** and **in-vitro** conditions. Since soft tissues are very compliant, non-homogeneous and anisotropic, accurate strain measurement requires special considerations.

This paper describes the development and application of particle tracking as a method for the non-contacting measurement of strain in soft tissues. Some advantages of the method are the redundant measurement of uniform strain - including shear strain -, quantification of the non-uniformity of deformation and little or no trauma to the tissue. Because the method is "digital", strains may be used for on-line control of experiments and large amounts of data may be analyzed facilitating a statistical approach to data analysis.

Our basic approach is to "track" the displacements of small markers placed on the unloaded tissue. Displacements at known particle positions or nodes are then used to construct interpolation functions approximating the displacement field over the measurement region. Strains follow directly from the strain displacement equations and these functions.

The strain measurement system consists of video cameras, video image digitizers and a high speed recorder. Factors such as strain rate, desired resolution, and the state of strain (plane vs. three-dimensional) determine the exact configuration of the system. Two setups are described for measuring strains in separate applications and results illustrative of the method are given.

METHODS

Small particles (50 - 200 microns) are used to mark at least three points on the tissue. Choice of particle size varies with the size of the region in which the strains are being measured and the expected magnitude of the deformation. The particles are attached to

the tissue using cyano-acrylate adhesive or, if sufficiently rough (e.g., silicon carbide), simply placed on the tissue surface. The centroids of the particles are used for tracking. Centroids are determined from a digital image of the particle using gray level information. Two different computer based approaches have been developed. In one, simply adding rows and columns of the matrix of gray levels which constitutes the digital image of the particle and searching for extreme values yields a good approximation to the location of the particle centroid [1,2,3]. More recently, images have been processed to increase contrast and the picture histograms used to set a threshold gray level. The result is a binary image of the particle and its centroid is easily found from its definition. The latter approach has the advantage of being closely tied to the image processing literature.

Measurements consist of particle displacements u and v in each of two orthogonal directions x and y measured from a reference state in which the tissue is unloaded. For n particles, u_i and v_i, the displacements at points (x_i, y_i), are known for i=1...n and a given state of loading. The displacements u(x,y) and v(x,y) may be approximated at interior points by

$$u(x,y) = f(\alpha_1...\alpha_n, x, y)$$
$$v(x,y) = g(\beta_1...\beta_n, x, y) \tag{1}$$

where f and g are polynomials in (x,y) and α_j (j=1...n) and β_j (j=1...n) are determined, for a given load, by matching expressions (1) to the known displacements of the particles.

The problem posed by (1) is comparable to the problem of developing a finite element stiffness matrix using the displacement method [4]. Thus we may write

$$u(s,t) = \Sigma h_i(s,t)u_i$$
$$v(s,t) = \Sigma h_i(s,t)v_i \tag{2}$$

where h_i (i=1...n) are the interpolation functions which map both the particle positions (x,y) and displacements (u,v) into the (s,t) plane. This is analogous to the isoparametric finite element. Thus

$$x(s,t) = \Sigma h_i(s,t)x_i$$
$$y(s,t) = \Sigma h_i(s,t)y_i \tag{3}$$

The strains follow from equations (2) and (3) by application of the chain rule to the derivatives associated with the strain measure employed (e.g., Green strain or engineering strain).

The choice of interpolation functions depends on the number of particles. Hoffman and Grigg [6], Humphrey et.al. [5] and Choi and Vito [3] chose bilinear interpolation with four particles for which the h_i are

$$h_1 = (1-s)(1-t)/4$$
$$h_2 = (1+s)(1-t)/4$$
$$h_3 = (1+s)(1+t)/4$$
$$h_4 = (1-s)(1+t)/4 \tag{4}$$

This is illustrated schematically in Figure (1). Note that since the interpolation is bilinear, the extensional strains vary quadradically in one direction and linearly in the other.
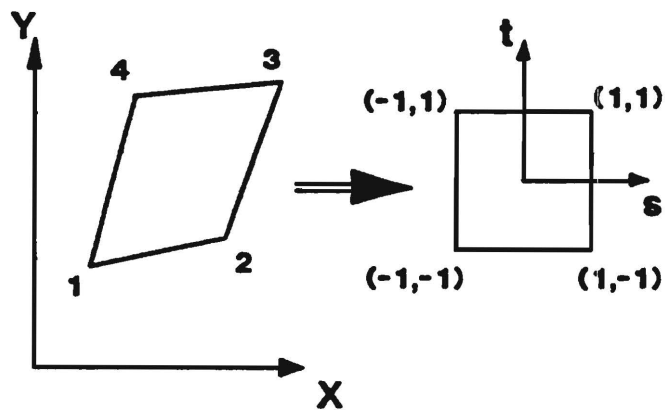

FIGURE (1) Schematic diagram showing mapping of (x,y) to the (s,t) plane.
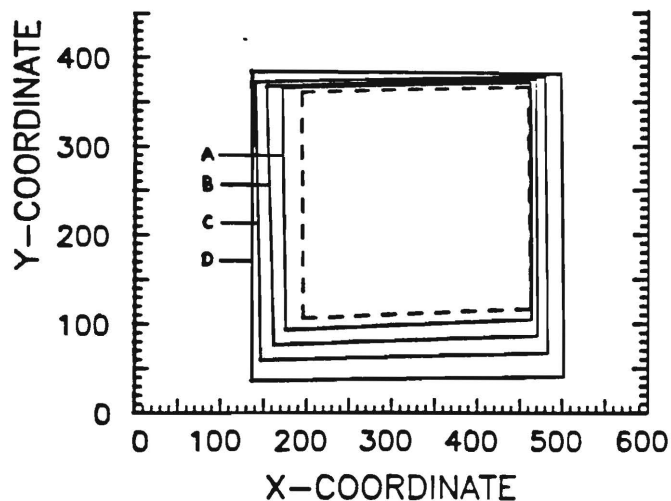

FIGURE (2) The deformation of four particles affixed to a sample of canine pericardium undergoing biaxial testing. The dashed lines represent the undeformed state. Strain fields for each of the four states shown are given in Table (1).
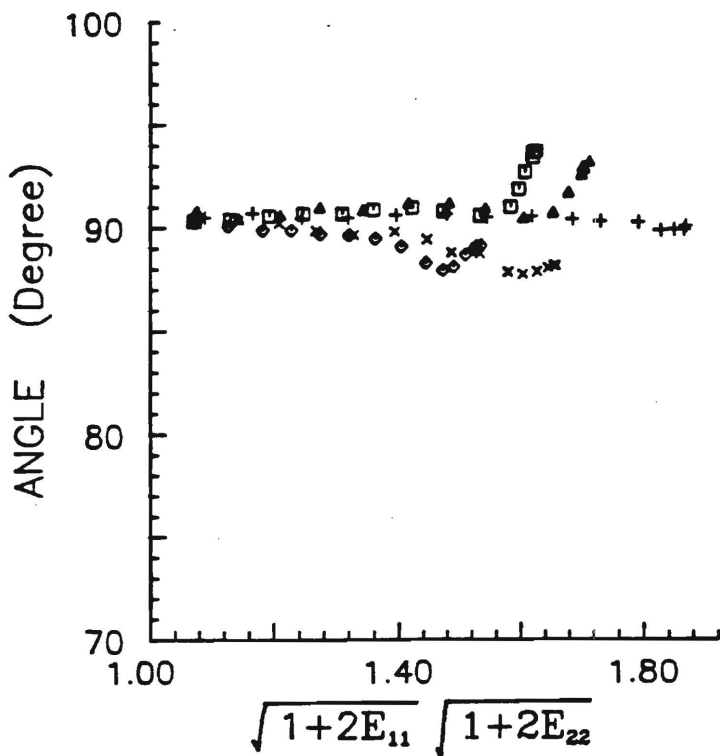

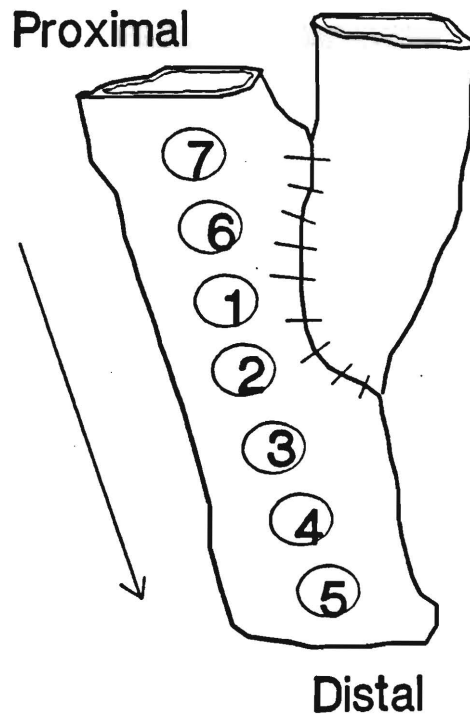FIGURE (3) Shear angle in pericardium undergoing biaxial loading.

FIGURE (4) Anastomosis geometry indicating sites at which strains were measured.

APPLICATION

Biaxial Testing of Pericardium

In previously published works on biaxial mechanical testing of soft tissues, the tissue was assumed orthotropic with the stretching and the material symmetry axis aligned. However, the material symmetry axis were usually unknown implying that shear strains were present in the tissue, even under equibiaxial loading. Video equipment has been used by others (e.g., [7]) to measure extensional strains in biaxial tests by tracking the edges of a marked rectangular region placed on a central part of the specimen. However, this method cannot be used to measure shear strains nor can it determine the degree of non-uniformity of the strain - both of which influence the choice of the mechanical model used to interpret the data.

Particle tracking has been used effectively to study the biaxial mechanical properties of the pericardium [3], the membrane which surrounds the heart. Interest in the pericardium stems from its role in coupling the left and right heart, its use in making heart valves and its constrictive function in pathologies such as pericardial effusion and pericarditis [8].

Figure (2) shows actual particle histories indicating the presence of shear strains. The system used could resolve 0.03mm and the accuracy of displacement measurement is +/- 0.06 mm. For finite deformation, the angle θ_{12} between the deformed differential line elements which were initially orthogonal to each other depends on both the shear and extensional strains. The cosine of θ_{12} is given by

$$\cos \theta_{12} = \frac{2E_{12}}{[(1 + 2E_{11})(1 + 2E_{22})]^{0.5}} \tag{5}$$

where E_{ij} are Green strains. Representative results are plotted in Figure (3).

Biaxial mechanical tests are analyzed using the theory of large elastic deformation [9] which assumes homogeneous deformation. Table (1) gives strains at the nodes as well as the center points for four values of loading.

Note that the deviation of the nodal extensional strains from the strain at the center point ranges from 3 to 17%. The small shear strains also exhibit considerable variation across the 1 cm square measurement region. This suggests that perhaps a finite element method ought to be used to analyze the data.

Strains in the Vicinity of an Anastomosis

Speculation in the literature (e.g.,[10]) indicate that graft compliance is a factor in determining the ultimate success of peripheral by-pass surgery. Since the strains in the arterial wall in the vicinity of an anastomosis are influenced by the elasticity of graft material used, studies are under way to measure the strain field in the arterial wall in the vicinity of an anastomosis. In experiments conducted in collaboration with the University of

Chicago, both PTFE and autogenous saphenous veins are used to produce end to side anastomoses in the femoral arteries of dog. Strains are measured using particle tracking. Particle tracking accommodates the expected rigid body motions of the arterial wall, geometric complexity, non-uniformity of strain and results in minimal disturbance to the measurement sites. Three particles (silicone carbide, approx. 50 μ) are placed at each of 7 measurement sites as shown in Figure (4). Although the deformation is three dimensional, the particles are placed close enough together (1 - 2 mm) so that out of plane displacements are negligible. For the lens used, the field of view was 2x2 mm and the depth of field about 100 μ at a working distance of 71 mm. Hence the strain resolution was 0.41 - 0.52% per pixel.

Data is recorded using a high speed video camera (240x192) at 60 frames per second or about 30 samples per canine cardiac cycle. Particle tracking is currently done by hand using a cursor to locate the approximate centroid of the particles every 1/30 second. Data reduction uses linear interpolation of the particle positions at each time step. From equation (1):

$$u(x,y) = f(\alpha_1...\alpha_n,x,y) = \alpha_1 + \alpha_2 x + \alpha_3 y$$
$$v(x,y) = g(\beta_1...\beta_n,x,y) = \beta_1 + \beta_2 x + \beta_3 y \tag{6}$$

At each time, the six constants $\alpha_1......\beta_3$ are determined by writing equations (6) for each particle. Thus, for each time step and for i = 1..3

$$u_i = u(x_i,y_i) = \alpha_1 + \alpha_2 x_i + \alpha_3 y_i$$
$$v_i = v(x_i,y_i) = \beta_1 + \beta_2 x_i + \beta_3 y_i \tag{7}$$

represent six equations in six unknowns. Linear strain-displacement equations are used since the strains, though superposed on large strains, are not too large.

Figure (5) shows the area dilatation at site #1 on the PTFE side vs time. Approximately 2 cardiac cycles are shown. Since the presence of shears in the vicinity of the sutures is a potential consequence of the compliance mismatch, Figure (6) shows the shear strain at site #2 on the veinous side.

To assess site to site and PTFE vs saphenous vein differences, data were reduced using three schemes for eliminating time. In the first, the maximum peak to peak strain was measured for a cardiac cycle. Secondly, the average strain over the 60 frames of data was computed. Finally, the amplitude of the first term of a Fourier series was computed. Figure (7) compares the amplitude of the first harmonic of the area dilatation on the PTFE side vs the saphenous vein side for various sites along the artery for subject #1.
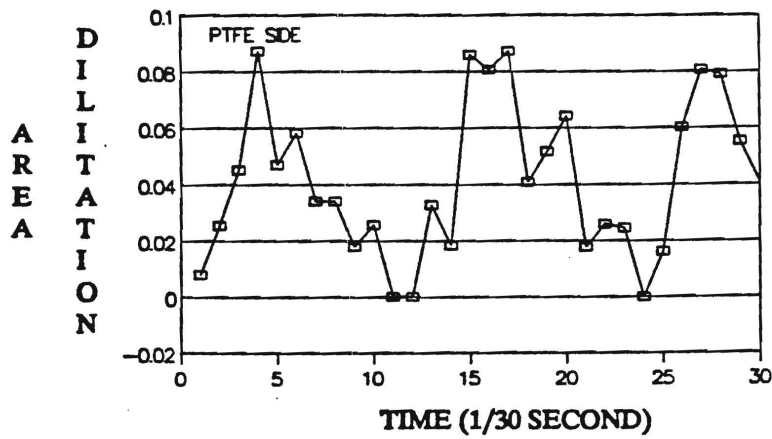
FIGURE (5) Plot of the area dilatation vs time at site #1 for roughly two cardiac cycles.
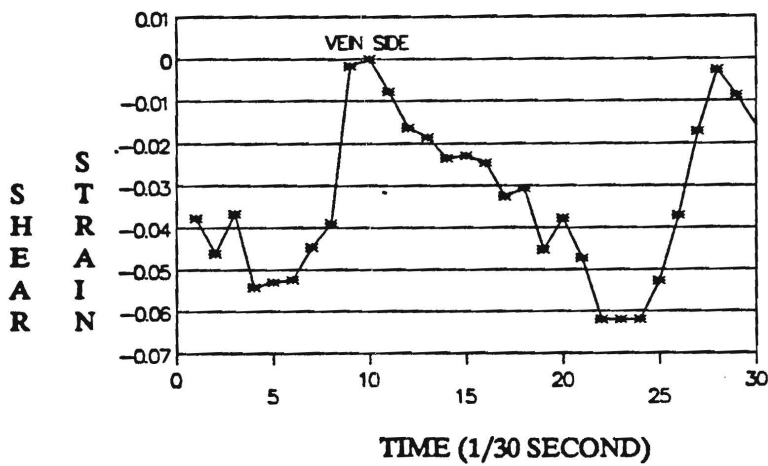

FIGURE (6) Shear strain for axis oriented along and perpendicular to the vessel centerline vs time for site #2, which is near the suture line.
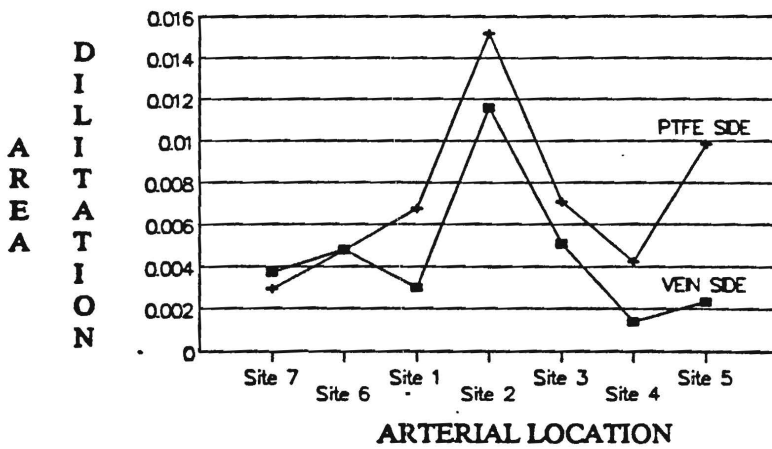

FIGURE (7) The amplitude of the first harmonic for various sites and for PTFE vs saphenous sides.

TABLE 1

Green strain values at nodel points (particle positions) and the center point. The 0.2 mm markers were placed on the central region (1 cm x 1 cm) of the specimen. The strains were calculated from the displacements of four particles using bilinear interpolation functions as described in the text.

Green Strains	Node 1	2	3	4	Center point	Deviation
E_{11}	0.082	0.082	0.098	0.098	0.090	±0.008
E_{22}	0.073	0.070	0.070	0.073	0.072	±0.002
E_{12}	-0.005	0.003	-0.005	-0.013	-0.005	±0.008
E_{11}	0.171	0.171	0.201	0.201	0.186	±0.015
E_{22}	0.156	0.169	0.169	0.156	0.163	±0.007
E_{12}	-0.018	-0.003	0.000	-0.015	-0.009	±0.009
E_{11}	0.293	0.293	0.312	0.312	0.302	±0.010
E_{22}	0.259	0.279	0.279	0.259	0.269	±0.010
E_{12}	-0.024	-0.015	0.010	0.000	-0.007	±0.017
E_{11}	0.435	0.435	0.426	0.426	0.431	±0.005
E_{22}	0.438	0.431	0.431	0.438	0.434	±0.004
E_{12}	-0.022	-0.029	0.025	0.031	0.001	±0.030

CONCLUSION

Particle tracking is a powerful method for the measurement of strain in soft tissues. The method has been successfully applied to **in-vitro** and **in-vivo** problems in tissue mechanics. The connection with finite elements and application to three dimensional problems have yet to be exploited.

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