PERCUTANEOUS AORTIC VALVE REPLACEMENT

This proposal for a project to develop a percutaneous aortic valve replacement is divided into seven sections. The section on anatomy describes the native aortic valve and its function. The following section on the valve's dynamics and physics discusses the implications of the anatomy for the valve's successful function. The sections on aortic stenosis and regurgitation describes valve dysfunction and the section on surgical therapy discusses current surgical replacement therapy and its problems. The final two sections outline the study objectives and stages. The purpose of the study is to develop a percutaneous placement technique and prosthetic valve that would mimic the function of the native valve and avoid problems associated with current methods for surgical replacement.

I. Aortic Valve Anatomy

The aortic valve directs the flow of blood from the left ventricle into the systemic circulation through the aortic artery. It accomplishes this function by opening during the contraction of the left ventricle and closing when the left ventricle relaxes.

In a normally functioning valve, three leaflet-shaped cusps open widely to allow the unimpeded transference of blood, and then close tightly, not allowing any blood back into the left ventricle. Significant restriction to blood flow is called stenosis, and blood leakage back into the left ventricle is called regurgitation.

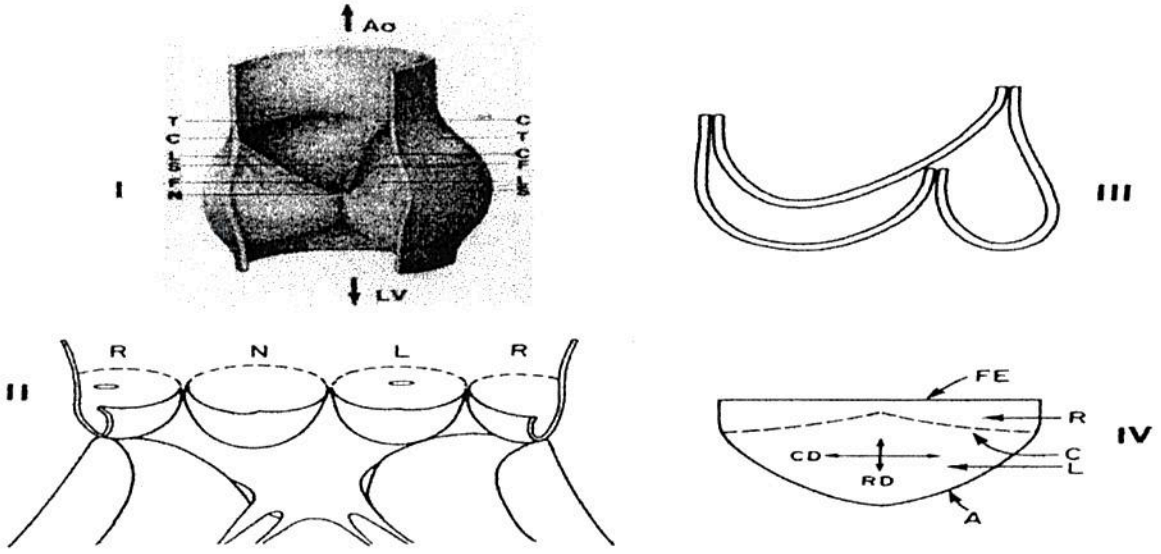


Figure 1

The aortic valve is a tricuspid structure. Each cusp folds up toward the aorta during the contraction phase and then folds back against the others in the relaxation phase. [Figure 1] However, it is important to understand that the structure of the aortic valve is complex, with integral relationships beyond its three-leaflet valve structure. For instance, each leaflet sits directly opposite an out pouching of the proximal aorta. This dilated segment, called the sinus of valsalva, is part of an anatomic relationship that assists the repetitive opening and closing of the valve while minimizing the stress on any point within this valvular apparatus. Further, the proximal portion of the aortic valve is highly elastic, which allows it to dilate during the contraction phase of the left ventricle.

Moreover, these valvular structures are integrally related to the coronary arteries, which supply blood to the heart. These arteries, as represented in Figure 2, are located within 2 of the three sinuses. Thus, each component plays a vital role in the function and durability of the valve.

The first components of the aortic valve I would like to discuss are the leaflets.

As stated, the number of leaflets within a normal aortic valve is three. Any congenital variation in the

number of leaflets causes significant problems with function. When there are less than three valves, the valve undergoes rapid stenosis and restriction. An individual with a unicusped valve rarely survives beyond the first year of life. Among individuals with congenital alterations in the valve number, the most frequently encountered is a bicuspid aortic valve. Individuals with this variation in valve number can survive into adulthood. However, this valve combination becomes more and more stenotic and regurgitant by the 4th and 5th decade, which usually results in the need for surgical replacement. (See figures 3 and 4). Rarely, an individual with a quadricusped valve will survive into adulthood. This alteration in design also results in marked stenosis.

The anatomy of a normal aortic valve (three cusps, sinuses, aortic arteries) permits the dispersion of pressure over a larger surface area in the structure.

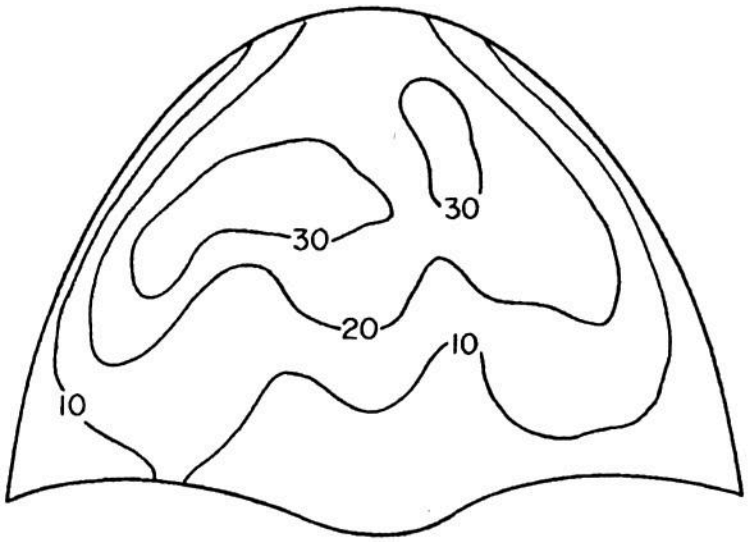


Figure 4.1

This dispersion resists the exhaustion of any one component of the valve. Moreover, the curvature of the

cusp structure allows the leaflet to reverse curvature, an ability needed in order to fold and allow the maximum opening diameter during contraction. Finally, a curved design allows a redundancy in the coaptation area of the leaflets. The area of coaptation is the valve edge that must meet and close in order to prevent regurgitation. Hence, both the number of leaflets and their overall shape is important in the function and durability of the valve.

As mentioned earlier, the valve leaflets have a direct relationship to the sinuses of valsalva. The sinus diameter is almost twice that of the aorta.

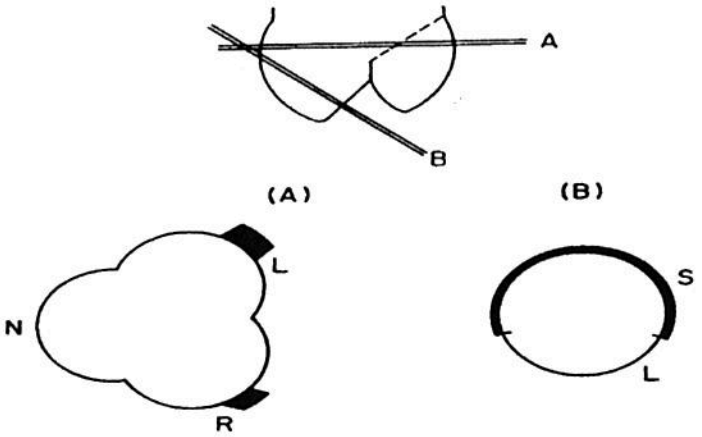


Figure4.2

This cavity plays an important role in the mechanism of valve closure.

[referenced Mano Thubrikar] An oblique section through the leaflet-sinus assembly shows this remarkable relationship (see Figure 4). This section reveals that the sinus and leaflet form a circle when the valve is in a closed position. Furthermore, it is angulated to a degree as to allow pressure transduction along the entire surface of this unit. All this suggests that the shape of the leaflet-sinus assembly is important in determining how stresses are developed within the valve. This relationship also allows the valve leaflets to close without straining the aortic valve. Finally, this relationship of the sinuses and valve allows for the efficient flow of blood in the coronary ostia.

Another structure, the aortic root, has been observed to expand during ventricular contraction. The dilatation of this structure reduces tension, which in turn reduces resistance to flow, as predicted by Poisselles' law, which describes the relationship of resistance to vessel diameter, length of tube and fluid viscosity. This phenomenon also allows for complete opening of the aortic valve. Interestingly, when the cusps open, a circular dimension is maintained that is at least the same diameter as before contraction(Medical Engineering & Physics 19(8): 696-710,1997). This behavior reduces circumferential stress on the valve and generates a reduced Reynolds shear stress number (the number used to evaluate the amount of stress in a confined fluid system). In a similar manner, the inner lining of the cusp of the valve, the lamina ventricularis, extends into the ventricular myocardium when the valve is in an open position. A confluence of fibers at the base, called the fibrous coronet, is a distinct structure separating the elastic fibers above and the myocardium below. However, this structure is not static. It is a very dynamic structure, which bends and molds to the forces exerted from the ventricular myocardium (Cardiovascular Research, 22,7,1988)(Journal of Biomechanics33 (6): 653-658, 2000 June). In a fashion similar to the aortic root, this structure allows the valvular apparatus to open with the least amount of strain.

The coronary arteries arise within or above the sinuses of valsalva. The blood flow to the heart occurs during ventricular diastole. At this time, the cusps of the aortic valve are closed, and as mentioned, the diastolic forces of the blood against the valve are dispersed along the valve and adjacent sinus. The opening, or ostia, of the coronary arteries, when located near the apex and middle of the sinuses, allows for least turbulent, most laminar flow characteristics.

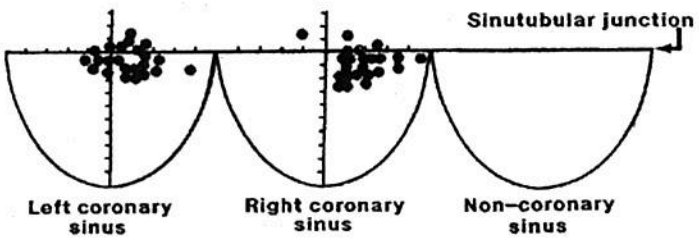


Figure 1-6. Coronary Artery Orifice—Variations. Diagram showing the location of the coronary orifices in a series of 23 normal heart specimens. The luminal aspect of the aorta is displayed. The markers represent tenths of the horizontal and vertical measurements in the sinuses. (Adapted from ref. 3.)

Figure 5

(This optimal location will be important to keep in mind when designing a replacement valve because this relationship promotes the greatest amount of flow with the least amount of resistance.) In disease states where these relationships are lost, it has been proposed that this loss could increase stress at the coronary ostia. [The Aortic Valve CRC press].

These integral relationships are not only seen in the gross anatomy of the valvular apparatus. The microanatomy shows the integral nature of these structures as well. The amount of elastin shown by staining methods is in a higher concentration here than anywhere else in the body(American Journal of Pathology 445 (7): 1931). This concentration allows a greater amount of dilatation of the structures in this area.

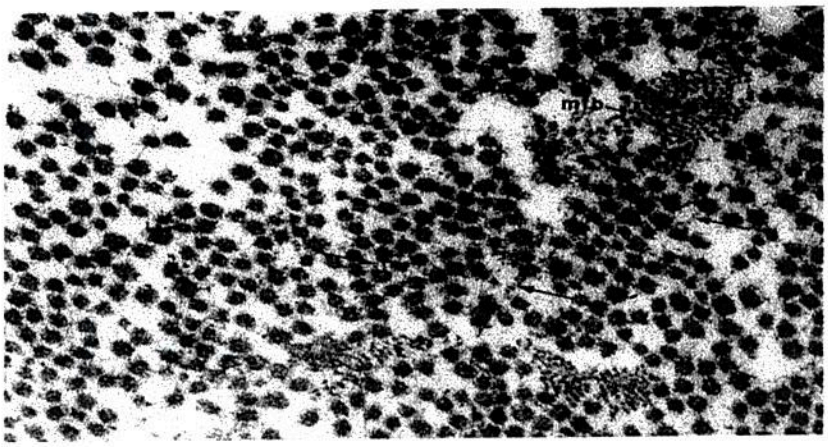


Figure 6

Further, scanning electron micrographs have shown the unique arrangement of collagen in the valves, which permits the unique reversal of curvature and is vital in the function of the valve. (See Figure 6). (Anatomic Embryology 172(61): 1985). The fibers are unusually small and arranged in sheets with unique distances between each strand. In theory, this would give a greater amount of tensile strength while allowing continued flexibility. As always, nature has selected the most efficient machinery, and we have only to discover the reasons why.

II. Aortic Valve Dynamics and Physics

The aortic valve is not a static structure. Full understanding of this structure requires understanding the dynamics and physics of the opening and closing of the valve: the motion of the various parts, the design of the valve in vitro and the hydrodynamics of the valve.

The valve's ultimate function is to allow fluid transfer from the ventricle to the systemic circulation. In order to do this efficiently, it minimizes shear stress, resistance to flow and tensile forces. The opening and closing of the aortic valve depends upon differential pressures, flow velocity characteristics and, as mentioned earlier, the unique anatomic relationship between the valves and the sinuses of valsalva.

The most comprehensive model of this process has been developed by Bellhouse et al. In this model, the flow of fluid through the aortic valve was studied by injecting dye into the flow of fluid. Some of the pertinent observations incorporated in this model were as follows: 1) The valve opens rapidly, and as the leaflets move into the sinuses, vortices form between the leaflet and the sinus walls; 2) The flow enters the sinus at the sinus ridge, curls back along the sinus wall and leaflet and flows then back into the main stream; 3) During the end of systole, the vorticeal motion forces the valves back toward a closed position. These observations are important because they show that absolute pressure

differences created between the aorta and ventricle are not the source of initial closure of the aortic valve. In fact, it would be detrimental to valve stress if these forces dictated closure of the aortic valve. For example, if two objects are separated and a set amount of force is applied to each, increasing the distance between them would produce greater velocity and the momentum at impact would be greater. Therefore, if the leaflets are closed or near closure as contraction is coming to an end, then the force used for coaptation would be less. Less force per cycle equates to greater longevity of the valve.

This phenomenon would affect the design for prosthetic valves. The cusps and the relationship of closure for prosthetic valves must incorporate passive closure during systole in order to lengthen the life span of any such device.

To understand how to do this, we must explore The theory of laminar flow as it relates to aortic valve function. Laminar flow is predicted by the Reynolds number, which incorporates the laws as described by Outsell and Bernoulli. In general, the lower the Reynolds number, the more likely that flow will be laminar. The equation that describes the Reynolds number in the aorta is as follows:

Ua/v = Reynolds number

That is U, which equals the velocity of blood and a, which represents the radius of the aortic valve, is inversely related to the viscosity of blood. As the velocity increases or the viscosity decreases, the tendency towards turbulent flow also increases.

Moreover, the behavior of the fluid in a system is predicted by the Strouhal number. In a system where viscosity, velocity and radius vary minimally, the rate of acceleration or deceleration of the fluid predicts laminar versus non laminar flow. When looked at in this perspective, it is easy to see the relevance of this information to valve function. Only a small pressure difference is required to open the native aortic valve.

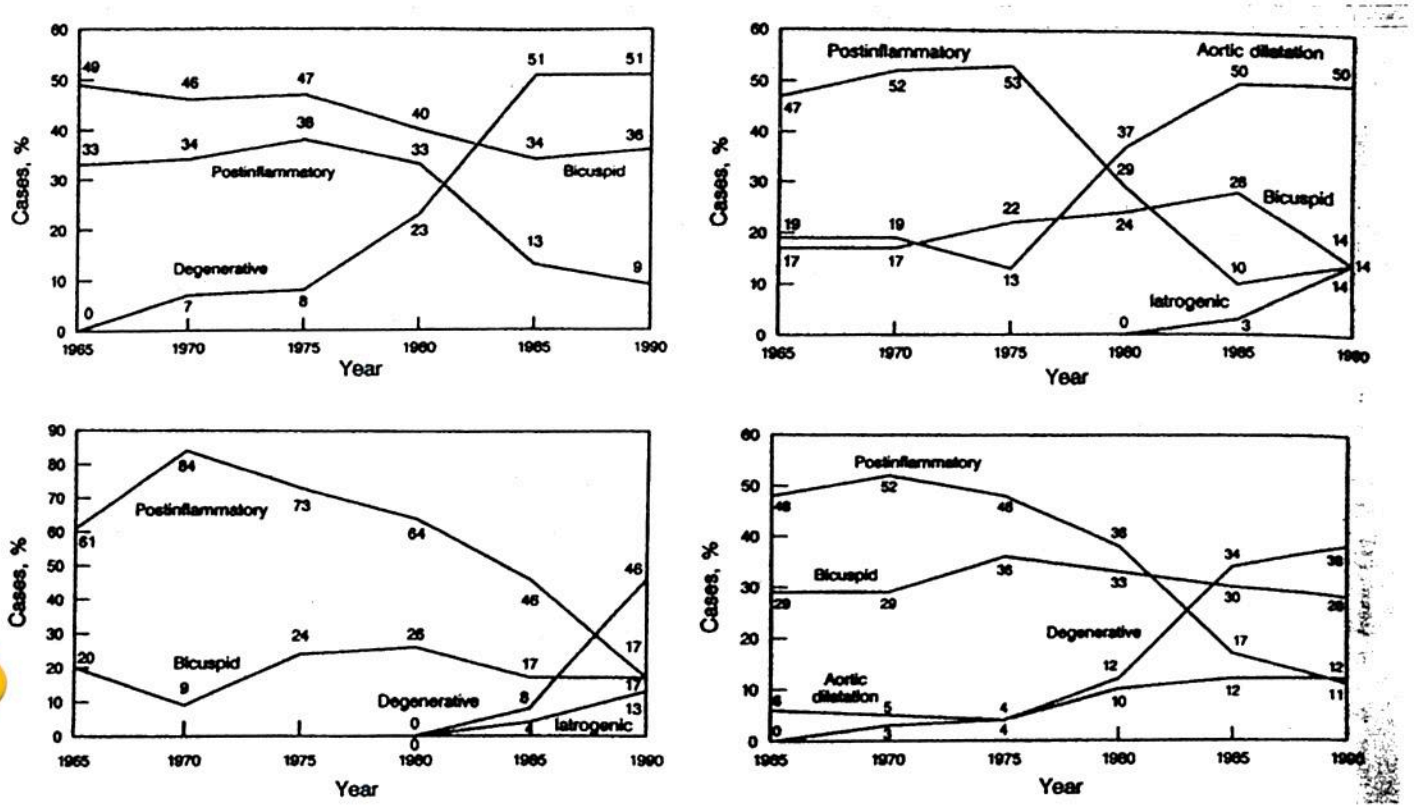
Maintaining a small pressure difference minimizes acceleration to flow. Thus, laminar flow is more likely. The deceleration phase is naturally a gradual process; however, as stated earlier, it is the relationship between the sinuses and the cusps that allows this deceleration to occur without an abrupt pressure drop. When laminar flow is produced, the resistance to flow, wall stress, shear stress and circumferential stress are reduced. This reduction decreases cardiac work and increases the longevity of the valvular apparatus. Ultimately, a design to replace a diseased aortic valve must incorporate many if not all of these relationships.

III. Aortic Stenosis

Aortic stenosis is the condition of restriction to the ejection of blood from the left ventricle to the systemic circulation at the aortic valve level. If the aortic valve cusps do not open, or there is failure of the valvular apparatus, then a pressure gradient develops. In order to overcome this pressure difference, the left ventricle begins to hypertrophy. Over a period of time, this process produces pressure overload on the left ventricle, which produces dramatic clinical symptoms. In the most severe form, it is fatal unless treated. The incidence of aortic stenosis varies considerably. In epidemiological studies, the incidence is between 2 to 4% of the general population.

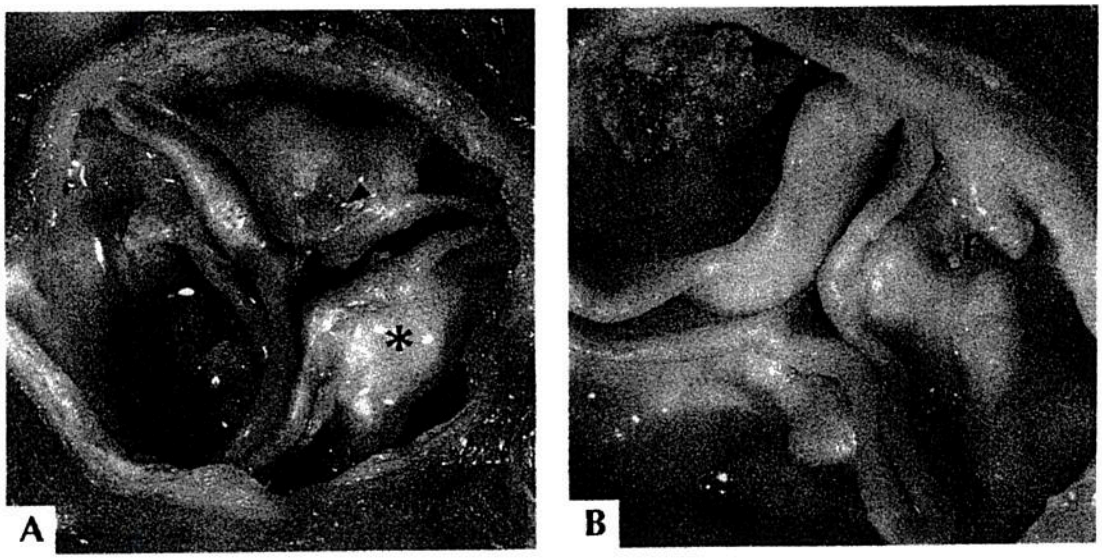
In the early 20th century, the most common etiology of aortic stenosis was rheumatic fever. This streptococcal infection produces inflammatory changes in the aortic valve. Interestingly, these changes affect the coaptation surface to a greater degree than the other structures of the aortic valve. Affecting the coaptation points results in fusion of cusps. This fusion results in a restriction to the opening of the cusps. A pressure difference develops as well as non-laminar flow. Once this cycle develops, valve deterioration and calcification increases. Unfortunately, post infectious aortic stenosis can result in rapid progression to severe aortic stenosis. Of the total cases of aortic stenosis

in the 1940's, reportedly 52% were the result of rheumatic fever. Currently, less than 9% of the cases of aortic stenosis are post inflammatory.



The second most common cause of aortic stenosis is a bicuspid aortic valve. This has remained relatively constant throughout the decades. It accounts for 33 to 40% of the total cases of aortic stenosis. This condition affects most parameters of aortic function because the optimal anatomic relationship between the sinuses, arteries and the valve cusp is lost. Further, the opening and closing characteristics of the valve are altered, which in turn alters the acceleration and deceleration of flow. As a result, non-laminar flow characteristics are developed. Because of the altered anatomy, a bicuspid aortic valve cannot easily reverse curvature. Due to this limitation, the bicuspid aortic valve has increased stress at the base. It is at this point where morphologic changes first appear. However, this valve is usually survived into adulthood.

Currently, the most common cause of aortic stenosis is degenerative aortic stenosis. By the 7th decade, the normal aortic valve can undergo degenerative changes. The characteristic that defines these changes is increased calcium deposition along the body of the cusps.



Predominantly the calcification is located at the bases of the cusp (see asterix in picture) and on the aortic side. When enough calcium is deposited as to restrict flow, then there will be a variable amount of fusion along the coaptation surface. The incidence of aortic stenosis reaches as high as 12% in octogenarians. This population accounts for 51% of the current cases of aortic stenosis. The factors that promote aortic stenosis in a normal valve are the same as those that contribute to atherosclerosis in arteries [nejm 1996]. Thus, degenerative aortic stenosis has become the most prevalent etiology.

Clinically, symptomatic aortic stenosis not only has disabling symptoms, but also a high mortality. Aortic stenosis is currently graded according to the calculated aortic valve area (see Figure7). As represented in the table, severe aortic stenosis occurs when the valve area is less than 1.0cm2 (AVA index of <0.6cm2/m2). The most

frequent symptom is angina pectoris, occurring in up to 70% of these cases. This is followed by syncope or presyncope. Once aortic stenosis becomes symptomatic, the 2-year mortality can be as high as 50% [Braunwal 1973]. The 10-year survival is a dismal 10%. In conclusion, aortic stenosis can produce severe life-limiting symptoms and ultimately is fatal.

Whatever the etiology of aortic stenosis, the proposed percutaneous valve offers a unique and beneficial approach to replacement.

IV. Aortic Regurgitation

Aortic regurgitation is the condition of leaked backflow of blood from the aorta into the left ventricle. This regurgitation results in a decreased effective cardiac output. In turn, longstanding aortic regurgitation results in an increased volume of work for the left ventricle. In time, the left ventricle begins to dilate. Unlike aortic stenosis, this condition can be well tolerated for many years. However, once the left ventricle begins to dilate and lose its contractility, it becomes rapidly symptomatic.

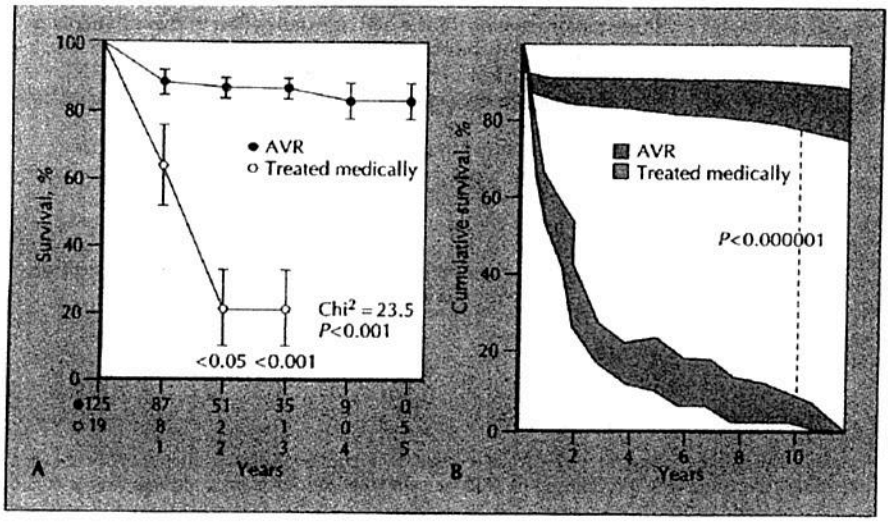
Etiologically, aortic regurgitation and stenosis are very similar. The most common etiology of aortic regurgitation has been rheumatic fever. However, just as in stenosis, this incidence has decreased as the incidence of rheumatic fever has decreased. Logically whenever there is stenosis, there can be increase circumferential stress placed upon the proximal aortic root. It is this stress that promotes aortic root dilatation in certain patients. Moreover, a dilatation of the aortic root can separate the cusps of the aortic valve and create regurgitation. Thus, senile aortic stenosis, bicuspid aortic valves and distinctly rheumatic aortic valves have a propensity to regurgitate. However, there are other unique entities, which promote aortic regurgitation. For example, Marfan's syndrome is

defined by defective collagen deposition. This deficiency manifests as dilatation of the aortic root at a very young age, and tragically can result in the dissection of the aorta. More commonly, the aorta can become dilated in response to systemic hypertension. In a certain portion of patients, aortic dilatation with concomitant aortic regurgitation is the only manifestation of their hypertension. Thus, there are distinctly different causes for aortic regurgitation in the presence of a structurally normal aortic valve.

Severe aortic regurgitation has a poor prognosis. Work by Goldschlager et al found that the survival of aortic regurgitation is about 50% at 8years (Am. J. Med. (54): 1973). With maximum medical therapy, it still has a poor prognosis. Even among asymptomatic patients, there is a decrease in the max Vo2 as measured with a standard cardiopulmonary exercise test. Moreover, many patients who undergo surgical replacement of the native valve for aortic regurgitation report an increase level of functioning that they didn't realize they had lost. In fact, although well- tolerated, aortic valve regurgitation is a serious disease, which limits a patient's lifestyle as well as life span.

V. Surgical Therapy

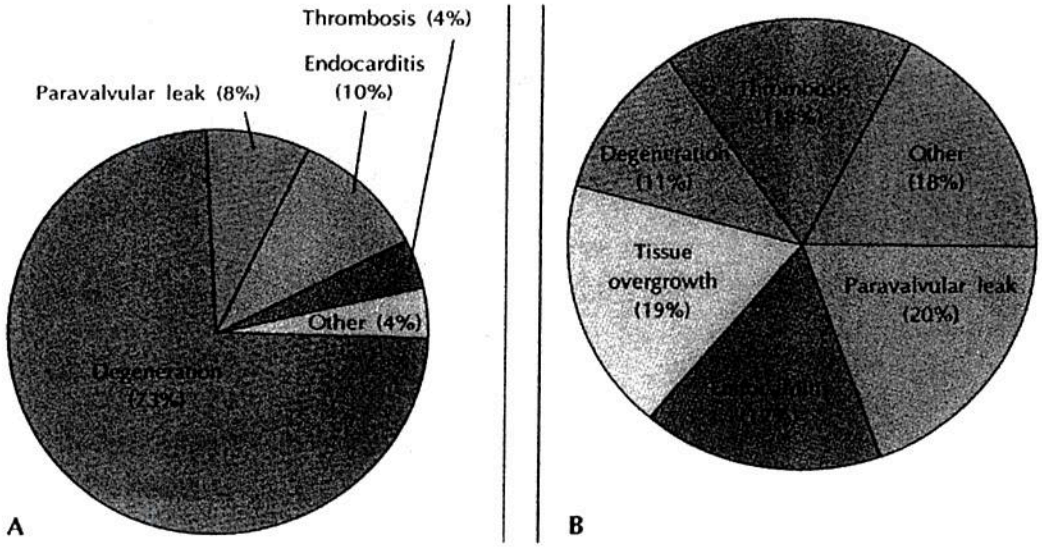
For patients suffering from aortic regurgitation or aortic stenosis, the best therapy to date is surgical valve replacement. There is no questioning the benefit of surgical vs. medical management for these conditions. The 5-year survival for medical treatment of symptomatic aortic stenosis is 20% vs. 80% with a standard valve replacement. The natural history of the valve has been well characterized by the work of Braunwald et al in 1973.



Unfortunately, aortic valve replacement carries certain surgical morbidity and mortality. Aortic valve replacement may be among the most invasive surgeries. It requires access to the native valve, which necessitates a sternotomy. Also, the heart must be stopped and placed on a bypass pump. Further, the ascending aorta is cross-clamped at a position proximal to the great vessels. The native valve is then excised, and depending upon the condition of the aortic root, it may be excised also. Then the mechanical or biomechanical valve (metallic vs tissue) valve is sutured into place. Although this is a life-saving procedure for those patients suffering from these disorders, the surgery is not without significant risk of mortality and morbidity.

The risks of the surgery can be classified into immediate and long-term risks. The immediate risks of the surgery involve the mechanics of the valve replacement procedure. In accessing the heart, the sternum is split in two by a reciprocating saw. Given that the sternum is a central point of attachment for the chest cavity, considerable effort must be applied to maintain the correct anatomic durability. The sternum currently is wired back into place with a series of interrupted suture wire from the cranial end to the dorsal end. Known difficulties encountered with this procedure are wound dehiscence and infection. The patients most at risk include diabetics, the immunosuppressed and the elderly. Wound dehiscence or

infection can be mild and readily amendable to simple wound care techniques. Or, these can be so severe as to lead to death or significant morbidity. The incidence is reported to be as low as 1 in 200 in low risk groups, and as high as 10 in 100 in high-risk groups.



Another immediate risk is a significant decrease in cerebral function. It is becoming more and more apparent that use of a bypass pump promotes cerebral dysfuntion. Under the best of circumstances, there is an immediate risk of major stroke reported to be 1 to 3%. However, among those patients without recognizable strokes, there are still reported deficits in cognitive function. When this cognitive dysfunction is measured in terms of IQ points, it can be dramatic. In one series, up to 60% of patients undergoing bypass surgery had an immediate drop in their IQ scores by 20 points. Family and friends often recognize a distinct drop in mental alertness. Thus, even in a technically successful surgery, there can be a substantial drop in cognitive function.

The long-term risks are also serious and include infectious endocarditis, thromboembolism and valve dysfunction. [expand and then discuss balloon valvuloplasty]

VI. The Study Objectives and Stages

The objective of this study is to demonstrate the feasibility of a percutaneously placed aortic valve as reflected in the testing of these 14 hypotheses. We speculate that the following assertions can be demonstrated to be the case:

1. A cross-linked nitinol expandable stent can be annealed to a biological valve (see appendix).
2. The flow characteristics produced by this uniquely designed device will perform in a similar fashion to that of other bioprosthetic valves.
3. The strain relationships will be proportionate to the native valve structure.
4. The flexible base will allow more even dispersion of flexion strain.
5. The interface of the stent aorta will be sufficient to maintain the valve in the proper position for function in-vivo.
6. The stent/valve can be inserted percutaneously.
7. The ascending aorta can accommodate a stented valve structure without rupture or significant dissection.
8. The ascending aorta and coronary arteries can be visualized with existing techniques.
9. With detailed visualization ,the stent/valve will be placed as to avoid obstructing the native valve function.
10. The stent/valve combination will not significantly obstruct coronary flow.
11. A biotome can be directed across the interatrial septum into the left ventricle.
12. Once a properly designed catheter is inserted into the left ventricle , the native valve can be excised in a controlled manner.
13. An animal would survive the placement of a percutaneous valve.
14. The stented aortic valve in vivo will have a

gradient of less than 10mmhg.

Our belief is that a properly designed valve can be placed nonsurgically without the assistance of a bypass pump and mimic the function of a native valve. The tasks of the study will be divided into 4 related stages: flow modeling, valve modification, catheter design and in-vivo experiments. These stages are discussed in detail in the following protocol

VII. Equipment and supplies

1. Lab associated equipment for the modification if needed of the existing valve. .
2. Nitinol wire
3. Nitinol soldering device
4. Template equipment
5. Aqueous solutions for the flow system
6. Preservation material
7. Dissection tools
8. Pig Hearts
9. Operating Room
10. Valve Flow Model with software
11. Statistical Software
12. Intracardiac echocardiography (Probes and Base)
13. Catheters
14. Biotomes and microengineering tools

VIII. Associates

1. Flow Modeling
   - Troy Norred MD
   - Steven Lombardo PhD
   - Frank Fu PhD
2. Valve Development
   - Troy Norred
   - Fu Fung Hsieh
   - Harold Huff
3. In Vitro Modeling
   - Troy Norred MD
   - Steve Lombardo PhD

Fu Fung Hsieh PhD

4. Procedure
   - Troy Norred MD
   - Timothy Catchings MD
   - Darla Hess MD
   - Wayne McDaniels PhD
   - Michael Sturek PhD

5. Editing and Data analysis
   - Troy Norred MD
   - Greg Flaker MD
   - Fu Fung Hsieh PhD
   - Steven Lombardo Phd
   - Timothy Catchings MD
   - Darla Hess MD
   - Frank Fu PhD
   - Wayne McDaniels PhD
   - Michael Sturek PhD

IX. Data Acquisition

1. Hemodynamics
2. Pressure gradients
3. Cardiac Output
4. Peripheral resistance
5. Dissection of the specimens
6. Histological Data
7. Morphologic data
8. Visualization Data
9. In-Vitro Modeling system
10. Histological sections

X **Budget**

1. Flow Model System

Laser Doppler Anometer	($1500.00)
Vivitec Flow Model	($13,500)
Software analysis System	($650.00)
Post-Doc Salary for 6 weeks	($3750.00)
Secretarial Time	($12.00/hr X25 hr/wk)
Sodium Iodide, glycerol, 1%water by volume	($75.00)

2. Valve Modification

Pig Hearts	($10.00/heart)

Slaughter House Material	($150.00)
Technician Processing Time	($17.00/hr)
Preservation Material	
Liquid Nitrogen	($25.00/canister)
Formalin	($5.00/6oz)
Clean up time	(17.00/hr)
Freezer Space Rental	($10.00/day
Lab Space Rental	(13.00/hr)
Nitinol Wiring	
Soldering Kit	($1950.)
Nitinol wiring	($950.00/ft)
Engineering Consultant Fee	($2500.00)
Technician and Physical Plant time	($25.00/hr)
Secretarial Expense	10 hours/week

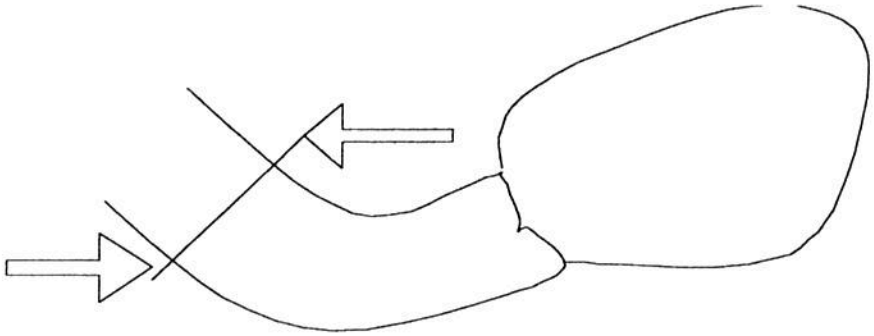
Experiment with Pigs

Pigs	($75.00/pig)
Fluoroscopic Time	($110.00/day
Technician time	($17.00/hr)
Lab expense	($500.00)
ACUVIEW SYSTEM	($30,000)
Catheters (variable if donated, but approx. $200.00)	
Data Software (included in Fluoroscopic room)	
Statistician Expense	($250.00)
Secretarial Time	(20hrs)

Total cost of for 6 week project

$66,610.00

Aorta Valve Modeling



DATA

ΔP_{max} = 300mmHg = 30cmHg

Q = 5liters/min = 5000cm3/min

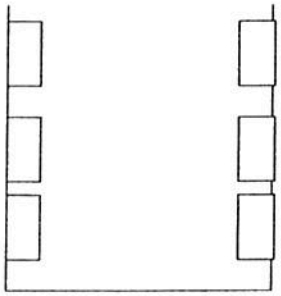
D = 3cm, R =1.5cm

σr >= 1200mmHg (rupture stress)

η (blood) = 1 cP = 0.01P

$A = \frac{\pi D2}{4} = \pi 9/4 = 7.1cm2$

$C = 2\pi r = 9.4cm$



Treat the aorta as a rigid capillary and the blood as a homogeneous liquid with viscosity of 1cP.

Some important quantities:

$\tau w = \frac{R\Delta P}{2L}$ shear stress at wall, L = length

$\bar{V} = \frac{Q}{\Pi R2}$ Mean velocity

$\gamma = \frac{4\ Q}{\Pi R2}$ Shear rate at wall

$\tau w = \frac{1.5cm \times 30cm\ Hg}{2\ (1cm)} = 22.5cm$

$Re = \frac{DVP}{\mu} = \frac{3cm * 12cm/sec * 1gm/cm3}{0.01g/cm/sec}$

$= 3600$ for blood, η=3cP

$= Re \approx 1200$

$\bar{V} = \frac{5000cm3/min}{\pi\ (1.5)2*cm2} = \frac{1min}{60sec} = \frac{12cm}{sec}$

$\gamma = \frac{4(5000cm3/min)\ 1\ min/60s}{\pi\ \ (1.5)3\ *\ cm3} = 30/sec$

The maximum stress upon the cusps when the vlave is closed is

$$Fmax = \Delta P*A = 30.0cmHg\ *7.1cm2 \approx 200cmHg/cm$$

To keep the rupture stress below 1200mmHg, we require a certain amount of stent/aorta interface area.

$$Fmax = \sigma r\ *\ A(stent)$$

If we specify that $\sigma r \approx 300mmHg$, then we need

$$200.0cmHg\ *\ cm2\ \ = 300mmHg\ *\ A(stent)$$

$\therefore$ A(stent) = 7.1cm2

Convert P = 300mmHg To MP2

$$300\text{mmHg} * \frac{1.0 \times 10(5)\ \text{P2} * 1\text{MP2}}{760\text{mmHg} \qquad 10(6)\text{P2}} = 0.04\text{MP2}$$

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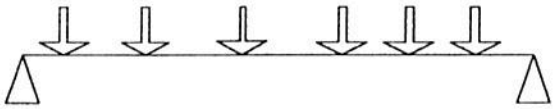
P1

Uniform load simply supported



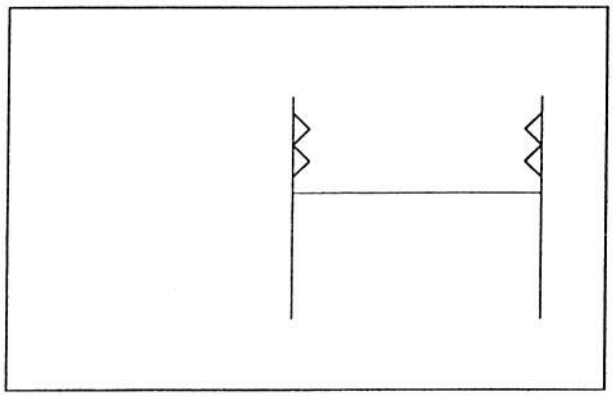
r =2

$$\frac{P1\ 2(4)}{Eh(4)} = \frac{1.016}{1-r} * \frac{Wo}{h} + 0.376\ (Wo)(3)$$

$$\sigma(qr) = \frac{Eh(2)}{2(2)} \left[\frac{1.238}{1-R(2)} \frac{Wo}{h} + 0.244(Wo)(2) \right]$$

Wo = 7.5 x 10(-6)m

σ(rq) = 8.4MP2



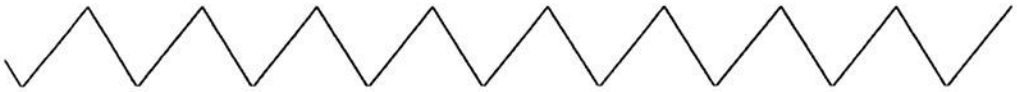
When the valve is closed, the maximum force is given by Fmax =ΔP *A. How is this force transmitted.

This stress must be opposed by a stress arising from aorta/stent interaction.

Since we know the aorta can withstand 30cmHg hydrostatic pressure (which is less than 120.0cmHg rupture strength), we will use $\sigma(r) = 30.0$ cmHg and thus

Astent = 7.1cm(2)

For stents of 1mm width, 10mmhigh and an angle of 60degrees



2 4 6 8 10

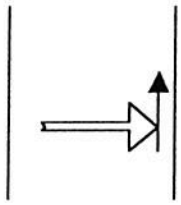
12 14 16 18 20

$\therefore$ 20 x 0.1 cm x 1cm = 2cm(2)

$\therefore$ NEED 4 APPROXIMATED STENTS TO WITH STAND 300mmHg

Friction must hold the stent in place

$$CoF = \frac{Ft}{Fn}$$



$Ft = Fmax = \Delta P * A = 30cmHg * 7.1cm(2) = 200cmHg/cm(2)$

The norma force exerted by the stent (which is opposed by the arterial wall) is

$$Fn = \frac{Ft}{Cof} = \frac{\sigma(r) * A(stent)}{Cof}$$

For the stent not to move, the normal force must exceed Ft/Cof

$$Fn > Ft/Fcof > \frac{\sigma(r) * A(stent)}{Cof} = \frac{200cmHg\ cm(2)}{0.20}$$

$\therefore$ If Cof > 0.20,

Fn = 1000cmHgcm(2)

$$\sigma n = \frac{Fn}{Astent} = \frac{1000cmHgcm(2)}{7.1cm(2)} = 140cmHg$$

Thus this approximates the rupture stress of 120cmHg (1200mmHg)

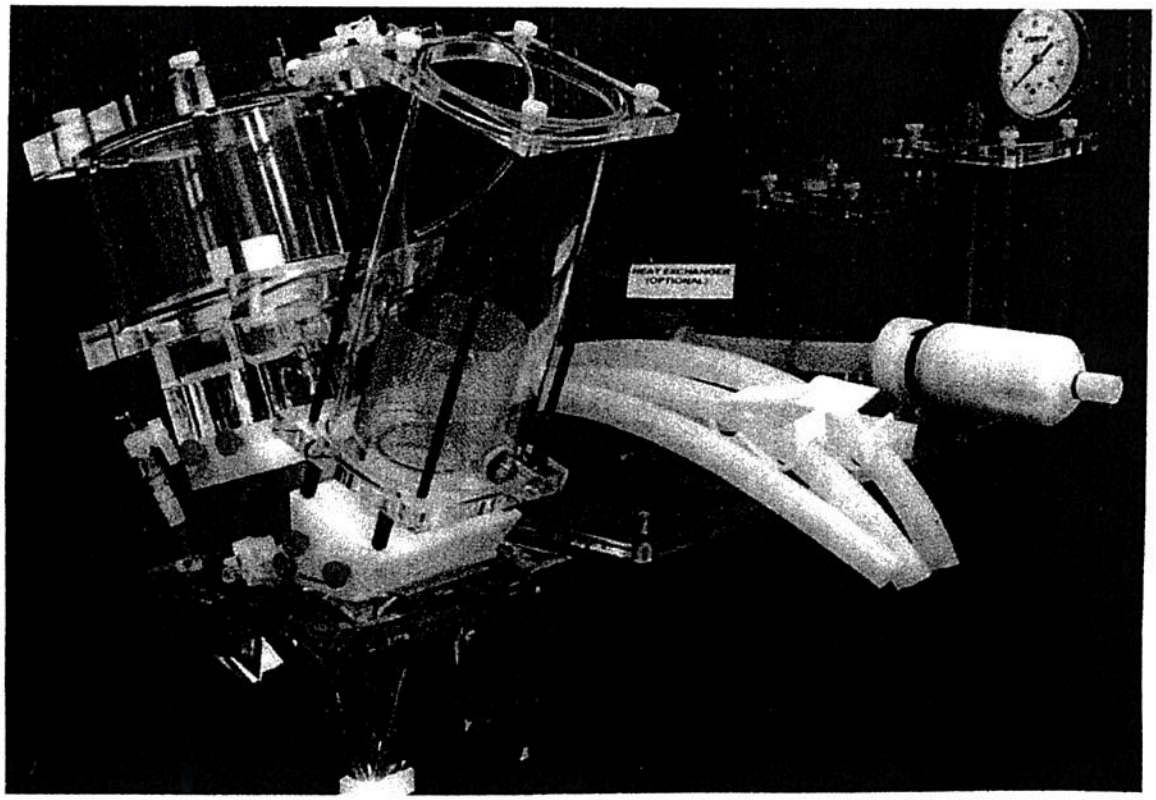
As you can see the amount of stent/aorta interface required for pressure far exceeding that physiologically required are easily achieved with a minimal amount of stents. This force naturally will only be required until the stent undergoes endothelialization.

4.

Protocol

Flow Modeling

The initial experiments will be performed to assess the valvular function in a flow model, which will be used to measure pressure and resistance (see adjacent picture).



The model is static and therefore will limit the assessment. However, important information about stress and strain relationships can be obtained. Basic measurements will be derived, and from these, we will publish our first data on the experimental valve.

The timeline for these experiments is expected to be 4 to 6 weeks. The preparation for these experiments will take up the majority of our project time. During this period, several mock runs will be used to modify the devices in order to obtain the most accurate hemodynamic information. Once we have accurate information concerning laminar flow characteristics, Reynolds number and strain relationships, we will begin to practice for in-vivo experiments.

Two types of flow systems have been developed, each with set points of measurements embedded at certain distances from the valve. One uses ultrasound sensors and the other laser sensors. In the pulsed laser system, the lasers are set at perpendicular angles to measure differential velocities. Further, these velocities can measure shear stresses along the systolic flow and regurgitant flow.

The flow systems allow high-speed photographs to be

taken to demonstrate the function of early closure in relationship to the sinuses (Annals of Biomedical Engineering. Vol. 26). We will be able to combine the flow model measurements and photographs to assess the affects of design variations. This final phase of the flow modeling experiment will help prepare for a more successful attempt at in-vivo placement of the experimental valve.

With current software available from Memry Corporation, we will have the data necessary to begin modification of the valve system before our in-vivo attempts. This software can help deduce strain relationships in a computer model. Differing values can be used to assess the effects upon the flow model system. These detailed in-vitro experiments will save valuable time and resources by troubleshooting prior to actual in-vivo experimentation.

Valve modification

The valve/stent combination has reached a point in design and development where successful modification depends on experimentation.

First, differing techniques of harvesting biological valves can have a dramatic impact on their function. When a valve is harvested and placed in formalin, it undergoes an amount of swelling from cellular death and necrosis, which can increase the thickness of the valve. Increasing the thickness of the valve can be detrimental to the placement by inhibiting the flow of blood into the coronary ostia. Similarly, cellular death affects valve longevity and function negatively . These factors necessitate experimentation with differing techniques of preservation in our initial valve development. We will try simple formalin preserved valves as well as cryopreserved valves. Differing buffering solutions may also be evaluated if found necessary.

The initial valve/stent design has several areas that may need modification. The most obvious of these is

the individual nitinol wire arrangement within the stent. For a number of reasons, it has been proposed that an interlaced series of nitinol wire would be favorable. For instance, it is the easiest technically to fabricate because it only requires looping the wires around a model and soldering them into place. This simplicity allows for rapid development and lends itself to modification when necessary.

The most commonly designed stents use a slotted tube arrangement. We may find this necessary in the stent/valve combination. I have employed the use of the physics lab to help in this pursuit if necessary. Further, through an engineer at Memry Corporation I have the ability to contract out the final laser cut of the valve out of a solid nitinol tube. This option will only be employed if it is found the expertise to accomplish this task is not available at this institution.

Differing designs can be employed to exactly set the relationship of an opening in the stented structure. Precise knowledge of the angle between the coronaries, the depth of the sinuses, the size of the cusps directly opposite the ostia and the degree in which the stented segments contour the ostia may be needed for the most effective percutaneously replaced valve. With the placement of the valve, it is crucial to allow enough distance between the native valve and the coronaries. Thus, there are several considerations in the modification of this valvular model. I have made several prototypes and find considerable variability in the interface of the stent and valve. Whether this variability will be important in the overall function of the valve is unknown at this time.

Furthermore, our initial experience reveals the meticulous nature of the annealing process. If a single suture is disrupted, the entire valvular apparatus can tear. Diligent work and documentation of the most effective way to anneal the two components of the valve

is necessary. Fortunately, much of this work has begun and many lessons have been learned, but more time and resources must be devoted to this line of modification. An estimate of one 40-hour week dedicated to this endeavor is realistic.

Another potential problem with a nonsurgically placed valve is perivalvular leak. If the edges of the valve begin to lift and form a low resistance channel, the valve may begin to develop torque upon itself, which may ultimately lead to valvular dysfunction and even failure. In addressing this hypothetical problem, it has been proposed to use a rim of perivalvular tissue to act as a counter valve, which seals itself hydrostatically and prevents or limits perivalvular leak. The in-vitro flow model will be invaluable in assessing this possibility. We will use the time at the end of the flow modeling stage to adjust for this possibility.

Of the many possibilities that have been entertained, the two most direct methods of limiting this leakage are root mimicry and pericardial sleeves. In the first method, the aortic root with the sinus morphology preserved will be attached to the proximal portion of the stented structure. Therefore, when the structure expands, the lateral force of blood will create a large surface to which the intima can adhere. This same concept may be applied to the pericardial sleeve. In comparison the pericardial sleeve may be more useful because it is more malleable and more easily sutured into the stent structure. It is readily apparent that a detailed evaluation of the valve function with each method will be needed before advancing to in-vivo experiments.

The final area for consideration of valve modification involves the deployment of the stented valve. Several potential problems may limit the expansion of a collapsed valve. [collapsed valve]

The most immediate concern involves the ability of the stent/valve connections to hold while expanding. Our initial experience has been favorable, but close evaluation of the valves has revealed micro-tears in the suture. These micro-tears obviously promote the

development of mechanical failure. Potential solutions to this problem involve differing suture techniques and bioglue to seal the valve before it is collapsed. Histological examination will be required when the in-vitro model is tested. After all these points have been addressed, we will proceed to in-vivo modeling.

Catheter Design

Percutaneous removal of a native aortic valve and placement of the experimental valve will require many novel catheter types. This design process will be kept very simple initially. We will use the largest catheters available in the initial in-vivo attempts. The catheters from outdated stock are unfortunately too small. However, contact with Cordis Corporation has produced some promising leads as to the availability of larger catheters. Further, the UMC Department of Engineering has facilities available for the development of new catheters. If needed, Dr. Lombardo and Dr Fu have the ability to liaison this portion of the experiment.

The in-vivo experiments will necessitate an entire system of native valve modification or extraction. I have designed different catheters that promote the percutaneous removal of the aortic valve. However, it is premature to divert much time to its perfection in the initial stages. As a matter of discussion, the most direct way of removing tissue is by biotome extraction. Several different catheter types have been proposed for this process, but the most useful will employ an anchoring device in to the thickened aortic valve. Initially, a catheter will be guided into the left ventricle via a transeptal approach. The catheter will be attached by a deployable screw into the native valve. This will allow the catheter to move with the valve. By moving with the valve, translational variation with movement will be minimized. For example, if a man is on a ladder that is swaying alongside a telephone pole which is also swaying, then making repairs on the line would be difficult. This is especially true if the two movements are independent of each other. However, if the man is connected to the pole, then the pole and the man move

with the same motion. To the man, it would appear as if the pole were stationary.

The same concept applies to extraction of a moving valve. With the device anchored, controlled sections of the native valve will be snipped out. It is unknown at this time whether complete removal of the aortic valve will be necessary. At a minimum, there will always be a rim of valve remaining on which the percutaneous valve will sit. Further understanding of the technique has made it apparent that simple aggressive debulking may accomplish the same task. Thus, both possibilities should be explored.

The design of the second set of catheters, those used to percutaneously place the valve, is a more ambitious project. The first of these set of catheters involve a system of rotablation. In this design, a catheter with two lumens is used to guide a rotablator device onto the native valve. The tip of the catheter has a roof of material to serve as a template guide. This allows the rotablator device to come into contact with the native valve and chip away the native structure. A continuous high-flow saline solution is directed into the return lumen of the catheter. This creates a venturi effect on the tip of the valve. The particulate matter is directed into the return lumen and back into a waste reservoir. However, if any particles escape, the size of the particle should be exceedingly small. This would naturally limit the amount of injury from peripheral embolization.

In-Vivo Experiments

The final stage of our experiments will involve the placement of the stent valve into an animal. This experiment will start with the detailing of the aortic valve anatomy. An intracardiac echoprobe (ICE) will be advanced into the right atrium, where a detailed view of the aorta is possible. The basic measurements of the root structures will include the valvular morphology and the description of the coronary ostia. Dr. Darla Hess

will be a collaborator in this area. From this description, the radius of the stent at final deployment will be known. This information will be used to individualize the stent to the experimental animals aorta. Also, the ICE will be used to measure the stent/aorta interface and the details of the experimental valve post deployment.

The initial design will use sacrificed animals. The animals will be put under anesthesia and peructaneously a catheter will be advanced into the ascending aorta through a sheath system. The valve is self-expanding and will be deployed by backing the catheter off of the stented portion of the valve. With the valve properly seated, a detailed recording of its function will be made by the intracardiac echoprobe. Also, basic hemodynamic data will be gathered. A transeptal catheter will simultaneously record left ventricular pressure with ascending aorta pressure recorded from the stent catheter. The animal will be maintained through the day and sacrificed after approximately 8 hours. The aorta and root structures will be analyzed histologically for evidence of intimal dissection and rupture. Given the limited amount of time, a living animal model will not be attempted in the initial experiments. However, the basic hemodynamics can be acquired, and this will be adequate to document the feasibility of the technique. The later experiments will include percutaneous removal and replacement of the native valve structure.

VII. Theory of Percutaneous Replacement

The understanding of the basic biological and physical properties of the aortic valve prompted my development of a novel approach to its replacement. As described in the following mathematical model, with an expanded stent placed into the ascending aorta, the interface provides a frictional force required to seat the valve firmly into position. Therefore, my model of a percutaneously placed aortic valve, utilizes the dispersion of force along a large surface area to

accomplish this critical task.

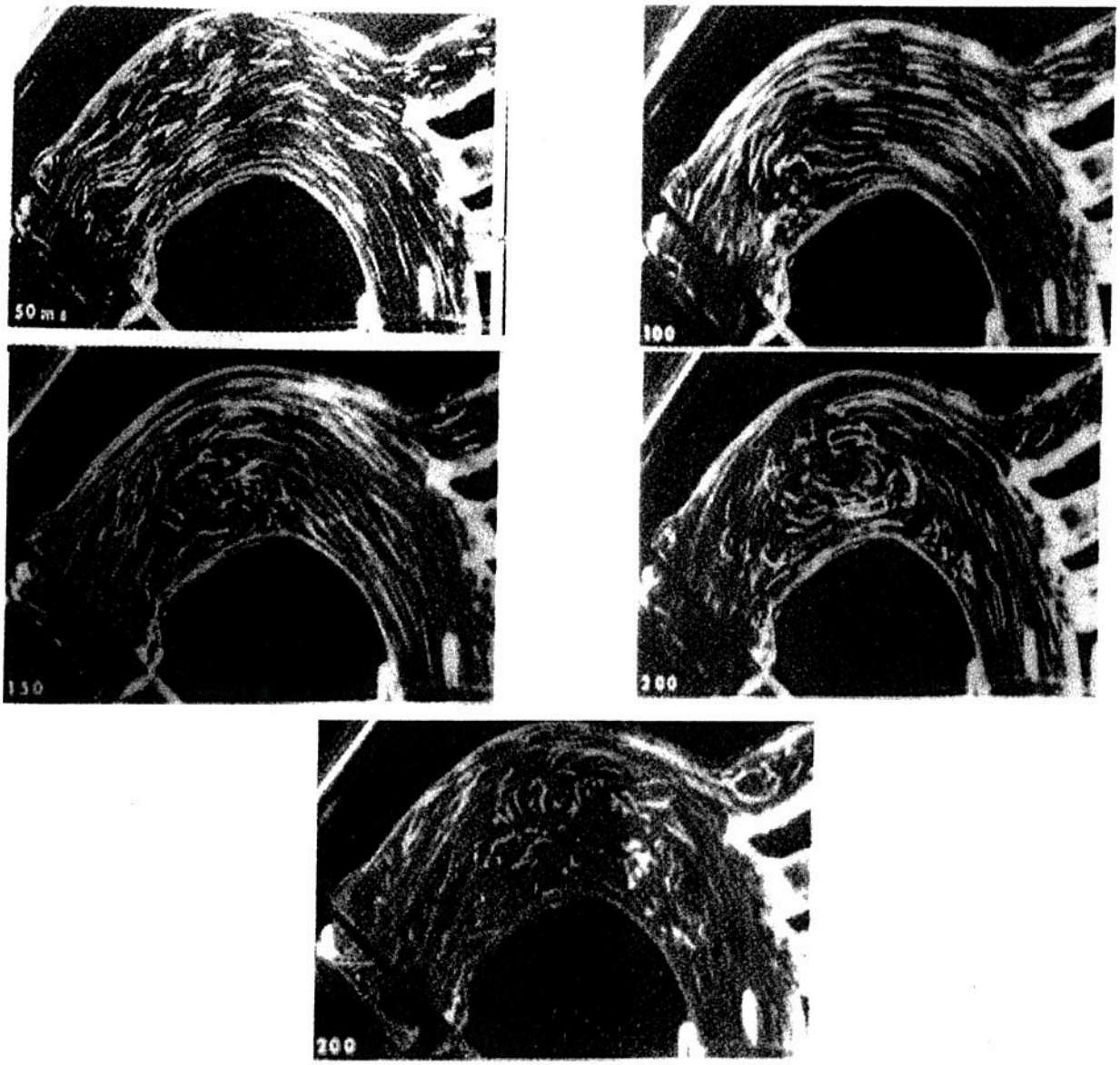
As you can see in the diagrammatic representation of the experimental valve, there is a stent made of nitinol wire connected to an extracted biological valve. As I have discussed, there are several types of patterns for this nitinol stent. My current models are an interlaced series of looped nitinol. This pattern has characteristics similar to a spring. As in a spring, it has a natural position that it maintains. Any force, applied to move the spring a certain distance from this position, is met with an opposite force proportionate to the distance it is displaced and the nature of the material of the spring. Further, if a fulcrum is applied at a certain point, the resistive force is inversely proportionate to the distance from the fulcrum. Both of these physical properties are important in the functioning of the experimental valve.

The spring-like characteristics of the valve facilitate its mimicry of the biological aortic root and associated structures. First, the base of the stent will be placed tightly within a very confined space. This constriction will act like a fulcrum. As stated above, the initial segment next to the fulcrum will have a greater degree of force resisting its deformation. The result is a proximally dilated segment. This dilated segment will approximate the dilatation of the sinuses of valsalva. Maintaining a cusp sinus relationship is important to the overall functioning of the experimental valve. Second, with accurate sizing, the stent can maintain its interface with the aorta at different radiuses. Obviously, the natural position of the expanded spring will need to be larger than the maximum diameter that the native ascending aorta can assume. A closer look at the parallels between the native valve and the experimental valve can be helpful in predicting its behavior in-vivo.

The encouraging parallels of this novel prosthetic valve with a native valve begin with the physical properties of memory wires as detailed above, and also

the mimicry of the geometric configuration that the experimental valve produces.

But by far the most important functional advantage of a stented/valve is the absence of a hinge or intraluminal obstruction. This problematic feature is found in all current mechanical valves. As shown in flow model experiments on these valves, [REFERENCE JOURNAL OF BIOENG #4] the initial 50msec of flow is fairly laminar but rapidly deteriorates to non-laminar flow patterns by 100msec. (see figures 10-14) The non-laminar flow characteristics are not limited to the immediate vicinity of the valve.



Interestingly, this turbulence, which is propagated into the great vessels, may have its own clinical consequence, but the literature is scarce in this area. Moreover, like the biomechanical valves this experimental valve does not obstruct flow. It is well published that biomechanical valves have the best flow characteristics. Thus, the benefits known to exist for biomechanical valves in terms of flow characteristics may apply to this valve.

It is also significant that the geometry of the cusps will not be limited in this valve model. The cusps undergo a unique reversal of curvature in the native valve. This reversal of curvature is promoted by contraction and flexion at the base of the valve. This property allows for the maintenance of a tubular geometry of the ascending aorta. Also, it promotes early closure by maintaining the sinus and cusp relationship.

In biomechanical valves, the base is rigid and not flexible. Reportedly, this inability to flex has biological consequences. For example, the important reversal of curvature is not allowed to occur. With the absence of reversal of curvature, all the stress/strain relationships are altered. The major effect is transference of a disproportionate amount of flexion strain to the bases of the valve. Experiments and morphological data from explanted valves have shown that the initial deterioration of biomechanical valves occurs at the bases. One possibility, in our experimental valve, which is flexible at the base, is that it will have less mechanical breakdown at the base and longer biological life.

The ascending aorta is said to have a barrow-like effect. This effect occurs when a segment of elastic tube dilates in response to initial flow of fluid into the tube. This function allows for the transfer of blood into the systemic circulation while lowering the resistance. In the elderly, much of this elastic effect is diminished. However, a reduced amount of dilatation still occurs and is important. The dilatation promotes lengthening of the valve in a circumferential plane as

opposed to a longitudinal plane. This behavior reduces the overall strain of the valve and promotes reversal of curvature. Again, in a flexible stented structure, the ability of the ascending aorta to dilate and retract will be maintained. This function is a favorable design characteristic of the experimental valve.

An important feature of the sinuses appears to be their load-bearing relationships with the corresponding cusps. This unique relationship may be the most critical. The sinuses are placed at an angle above the corresponding cusp. The valve leaflets and the corresponding sinuses form near perfect circles. This dramatically increases the surface area in which the systemic pressure can be dispersed. In pressure models it is shown that the pressure is evenly distributed. Thus, no one area of the valve is subjected to an abnormal strain. Further, the base of the valve is located at a position between the sinuses and the cusp. It is this property that acts as a mid-fulcrum between the two structures. Simply put, the pressure in the sinus offsets the pressure on the corresponding cusp. This relationship guards the cusp from prolapse. The experimental valve has a sleeve of tissue extending into the ascending stent. This tissue serves the purpose of limiting edge regurgitation and also counterbalances the pressure of the systemic circulation as does the native valve.

Two less obvious entities and functions of the aortic valve involve the transmission of blood flow to the coronaries in diastole and the preclosure of the cusps. When the valve is in opposition of the sinus, the flow in the coronaries is maximized. In animal models where this relationship is lost, the flow characteristics are less laminar. Further, to promote longevity of the valve, the cusps need to close as ventricular systole ends. As mentioned, if the cusps are fully open to a 75-degree angle when flow is reversed, a force over a distance is developed, and the coaptation surfaces would hit each other with greater momentum. This would logically produce greater wear at the coaptation

surfaces. Within the native valve, as discussed earlier, this mechanism of preclosure is maintained with relationship of the sinuses and cusps. Thus with a flexible and anatomically preserved valve, early coaptation wear and maximized coronary flow should be maintained.

It is in consideration of these valuable parallels between the native valve function and the experimental valve that I submit this valve to undergo further scientific scrutiny. The experimental valve offers theoretically better overall function with a minimized risk.

To summarize in a brief narrative, the valve has several advantages over the existing surgically placed valves. First, it can be placed nonsurgically which will limit the time needed for recovery. Second, it can be done without the assistance of a bypass pump. Third, it will obviate the need for anticoagulation and its risks. Lastly, it may offer an option to certain patients where surgery is not possible.

X. Aorta Valve Modeling

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cut passages

Pargraph One: Historically, it has been theorized that this characteristic reduces the amount of work that the left ventricle performs. However, this simplicity should not mask the complex nature of the valve.

Paragraph Three Coherence- - - - - - BEGIN DISCUSSING SHAPE OF VALVES OR STILL DISCUSSING 1-2-3-4 variation?

Further, the cusps in this quadricusped valve exhibit a defined convexity.

....

1. Physics and equations
2. Mathematics
3. Dispersion of Force/area
4. Maintenance of normal anatomic relationships

a. Flexion
b. Reversal of curvature
c. Barrow effect of the proximal aorta
d. Dispersion of Forces along the sinuses
e. Increasing flow characteristics of the coronaries
f. Eddy currents in the sinuses promotes early closure and reduces wear
g. Favorable strain characteristics
h. Laminar flow preservation

LIST OF CV'S

CURRICULUM VITAE

TIMOTHY T. CATCHINGS, MD., F.C.C.P.
10410 Snow Point Drive
SSN: 254-88-5590
Bethesda, MD 20814
Permanent Home Telephone: 301-530-8550
Temporary Home Telephone: 573-442-1131
Office Telephone: 573-882-2296
Fax: 573-884-7743

PERSONAL INFORMATION

Birthdate/Place:
December 30, 1952 – Mitchell Co., GA

Marital Status:
Married to Cynthia Blaylock

Children:

Christopher (1970)
Christi Dawn (1976)

EDUCATION

College:

Albany State College, Albany, GA, 1970 – 4, B.A. Chemistry.
Harvard University, Cambridge, MA, Summer Semester, 1972.

Medical School:

Emory University School of Medicine, Atlanta, GA, 1974 – 8, Doctor of Medicine 1978.

Postgraduate Training:

Medical Internship, Medical College of Georgia Affiliated Hospitals, Augusta, GA, Internal Medicine, 1978 – 9.

Internal Medicine Residency, Naval Regional Med Center, Portsmouth, VA, 1980 – 2.

Fellowship in Pulmonary Diseases, Naval Hospital, Portsmouth, VA, 1982 – 4.

Pulmonary Pathology, Armed Forces Institute of Pathology, Washington, DC, Oct – Nov 1983.

Critical Care Rotation, Bowman-Gray School of Medicine, Winston-Salem, NC, 1984

Fellowship in Cardiovascular Diseases, National Naval Medical Center, Bethesda, MD, July 1995 – May, 1998.

Fellowship in Cardiovascular Diseases, University of Missouri-Columbia, July 1999 – July 2000.

OTHER

Intermediate Level Leadership & management Training Course, Naval School of Health Sciences, Portsmouth, VA, April 1986.

Airborne Infantry Training, Ft. Benning, GA, January 1995.

Cardiopulmonary Exercise Testing, UCLA-Harbour, Torrence, CA, March 1996.

HOSPITAL STAFF AND UNIVERSITY POSITIONS

Assistant Professor of Medicine, University of Missouri-Columbia, July 2000 – Present.

Director Coronary Intensive Care Unit, University of Missouri-Columbia, July 2000 – Present.

Staff Pulmonary Physician, Naval Hospital, Portsmouth, VA 1984 – 7.

Staff Internist, Portsmouth Psychiatric Center, Portsmouth, VA, 1984 – 7.

Director, Intensive Care, Naval Hospital, Portsmouth, VA, 1986 – 7.

Medical Staff, Medical Center of Central Georgia, Macon, GA, 1987 – 1993.

Associate Director of Critical Care, Medical Center of Central Georgia, Macon, GA, 1987 – 1993.

Chairman, Department of Medicine, Medical Center of Central Georgia, Macon, GA, 1991 – 2.

Division Chief Pulmonary and Critical Care, Mercer University School of Medicine, Macon, GA, 1991 – 3.

Director, Nutrition Support Team, Medical Center of Central Georgia, Macon, GA, 1991 – 3.

Associate Professor of Internal Medicine, Mercer University School of Medicine, Macon, GA, 1987 – 1994.

Associate Residency Program Director, Department of Internal Medicine, Mercer University School of Medicine, Macon, Georgia, 1992 – 3.

Associate Professor of Anesthesiology, Mercer University School of Medicine, Macon, GA, 1991-4.

Advisor to the Dean of Minority Affairs, Mercer University School of Medicine, Macon, GA, 1991 – 3.

Faculty Advisor to Student National, Medical Association, Mercer University School of Medicine, Macon, GA, 1991 - 3.

Assistant Professor of Medicine, Uniformed Services Universtiy of health Sciences, Bethesda, MD, 1995 – 9.

Current Position: Staff cardiology attending, University of Missouri-Columbia, Columbia, MO, 1999 – Present.

HONORS/AWARDS

Outstanding Clinical Faculty Member, Mercer University School of Medicine, Class of 1990, June 1990.

Outstanding Clinical Faculty Member, Mercer University School of Medicine, Class of 1991, June 1991.

Faculty Selected for Hooding Ceremony, Mercer University School of Medicine, Class of 1991, June 1991.

Honored for Outstanding Service as Department Chairman, MCCG 1991 – 2, Department of Medicine, 1993.

CERTIFICATIONS/LICENSURES

Board Examinations:

Diplomat American Board Internal Medicine, 1982.

Diplomat Certified in Pulmonary Disease, 1984.

Fellow American College of Chest Physicians, 1986.

Diplomat American Board of Internal Medicine, Critical Care Medicine, 1987.

Licensures:

License State of Virginia (#37149)

License State of Georgia (#30030)

License State of Missouri (#1999134580)

DEA# BC1247661

Certifications:

Certified Instructor Advanced Cardiac Life Support (ACLS)

Certified Advanced Burn Life Support (ABLS)

Former Instructor Advanced Trauma Life Support (ATLS); Current Provider Certification.

MILITARY

Current Rank:

Retired Captain, Medical Corps, USNR

Duty Stations:

USS Sylvania, AFS-2, 1979 – 1980.

NRMC, Portsmouth, VA, 1980 – 2.

Naval Hospital, Portsmouth, VA, 1982 – 7.

Director Medical Services, Fleet Hospital 14, Headquarters, Jacksonville, FL, 1990 – 2.

Naval Reserve Centers, Macon/Atlanta, GA, 1987 – 1995.

National Naval Medical Center, Bethesda, MD, 1995 – 9.

PROFESSIONAL SOCIETIES (past and present)

American College of Chest Physicians
Society of Critical Care Medicine
American Medical Association
Bibb County Medical Society, Macon, GA
National Medical Association
Virginia Thoracic Society Member

Washington Critical Care Society

PUBLICATIONS

1. Catchings, T.; Prough, D.: *Symptoms of Clinically Silent Intracranial Mass Lesions Precipitated by Treatment with Nifedipine.* Surgical Neurology, 1985; 24: 151-2.

2. Catchings, T.; Beamer, W.; Lundy, L.; Prough, D.: *Adult Respiratory Distress Syndrome Secondary to Ethylene Glycol Ingestion.* Annals of Emergency Medicine, 1985; 14: 595-6.

3. Joiner, A.; Suner, J.; Catchings, T.: *Unilateral Diaphragmatic Paralysis Secondary to Carbon Monoxide Poisoning.* Chest, 1989; 97: 98-9.

4. Chipley, P.; Castresana, M.; Bridges, M.; Catchings, T.: *Prolonged Use of an Endotracheal Tube Changer in a Pediatric Patient with a Potentially Compromised Airway.* Chest, 1994 ; 105: 961-2.

RESEARCH

CHESS Trial, HA-1A, Centocor, Inc., Principal Investigator, Medical Center of Central Georgia, Macon, GA, 1992 – 3.

Measurement of Carbon Dioxide Stores in Normal Adults. Exercise Physiology Lab of Harbor-UCLA Medical Center, Torrence, CA, Fall 1997.

COMMUNITY SERVICE

Sponsor of Cecil T. Catchings, I. Scholarship fund, Camilla, GA, 1989 – 2000.

Contributor to Children's Hospital, Medical Center of Central Georgia, Macon, GA, 1990.

Contributor to Macon Rescue Mission, Macon, GA, 1989 – 1992.

Contributor to Macon Outreach, Macon, GA, 1990 – 2.

Volunteer to Roberta Bowman Chapter Eastern Star Community Service, Macon, GA, 1989 – 1990.

Stephen J. Lombardo

Department of Chemical Engineering, University of Missouri, Columbia, MO 65211
(Phone: 583-884-1644, Fax: 583-884-4940, E-mail: lombardoS@missouri.edu)

EXPERIENCE

1997-present **University of Missouri, Columbia, MO**

Assistant Professor. Research areas in the development and processing of ceramic materials for structural, membrane, and electronic applications. Research programs in powder synthesis, slip casting, sintering, and characterization of materials.

Funded Projects(title, sponsor, total award, dates, % of total credit)

1. Dilatometry and Mass Spectrometry Study of Ceramics,

University of Missouri Research Board, $50,000, 7/98-6/99, (100%)

2. Fabrication and Characterization of High Voltage Capacitor Materials
   AlliedSignal, $69,830, 11/1/98-8/1/99, (100%)

3. Studies on Binder Burnout and Modeling,
   AlliedSignal, $63,463, 11/1/98-8/1/99, (100%)

4. Use of Quasi-Elastic Neutron Scattering to Characterize Molecular Motion in Ultramicroporous Ceramic Membranes,
   Petroleum Research Fund, $25,000, 6/1/99-5/31/01 (100%)

5. REU Supplement to "Diffuse Ultrasonics and Materials Characterization"
   NSF-REU, $10,000, 3/1/99-11/30/99, (25%)

6. REU Supplement to "Diffuse Ultrasonics and Materials Characterization"
   NSF-REU, $12,500, 9/1/99-8/31/00, (25%)

7. Addressing Different Learning Styles in Thermodynamics with Graphical Simulations,
   NSF, $74,676, 6/1/99-8/31/00, (7.5%)

8. Experimental and Modeling Studies of Binder Removal Using Supercritical Extraction,
   Honeywell, Inc., $49,975, 2/10/00-9/30/00, (50%)

9. Fabrication and Characterization of Capacitor Materials with High Breakdown Strength and High Dielectric Constant,
   Honeywell, $50,000, 10/1/00-9/1/01, (75%).

10. WEB-Based Lab Procedures for Chemical Engineering 170: Principles of Chemical Process Measurement,
    MU Alumni Association, $500, 8/1/00-12/31/00 (100%)

1996-1997 **CeraMem Corporation, Waltham, MA**

Research Group Leader. Proposal and execution of government-funded research projects covering the development of novel functionally-graded ceramic materials for use as high-temperature seals. Program Manager on contracts for developing ceramic and polymer membranes and new membrane processes for microfiltration, pervaporation and gas separation.

1992-1996 **Norton Company, Worcester, MA**

Worldwide manufacturer of ceramics, abrasives, and materials; wholly owned subsidiary of St. Gobain, a $20B French company.

Research Associate, Crystar Diffusion Components 1995-1996
Provide R&D management($1.2MM budget) and technical direction for business supplying recrystallized silicon carbide diffusion components to semiconductor industry.

- Managed R&D effort for providing a replacement wafer to the electronics industry; prototypes in evaluation at customer sites are exhibiting extended life.
- Evaluated and summarized strategic position of SiC purity for next generation products
- Developed fundamental models describing infiltration mechanisms in porous media; principal results confirmed by experimentation.
- Assessed use of non-destructive methods for determining product quality and origin of defects; identified role of defects in product failures.

Group Leader, Ceramic Processing Group, Northboro R&D Center 1994-1995
Managed R&D group providing corporate-wide processing and materials services to individual business units. Full P&L and planning responsibility. Program manager and principal investigator on $1.2M government contract developing "Ceramic Solid Free Form Technology" using photo-gel polymers. Experience in forming techniques.

- Improved product yield of an extruded zeolite honeycomb catalyst from 25% to 65 %.
- Used a gel forming technique to fabricate microabrasive components with a 4-fold improvement in abrasive performance.
- Performed comprehensive characterization of the dielectric properties of grains and their mobility in electric fields; report has served as a blueprint for subsequent work.
- Developed a heat and mass transfer model for identifying feasible methods for heat removal during grinding processes.
- Exceeded the profit plan by 20 % during a difficult financial period.

Senior Research Engineer, Ceramic Processing Group, Northboro R&D 1992-1993
Provided processing and characterization of ceramic materials. Principal investigator on government contract for "Reliable Ceramic Processing."

- Synthesized first monolithic samples of boron suboxide material and determined the bulk mechanical properties; led a team effort to prepare an ATP proposal.
- Developed a model to identify methods for minimizing density gradients in pressure cast components.
- Optimized the material properties of silicon carbide for use as a Read/Write head substrate in hard disk drives; led to first functional heads from this material.

1991-1992 **Fritz-Haber Institute of the Max-Planck Society, Berlin, Germany**
Department of Physical Chemistry, Government sponsored research lab

- Characterized adsorbates, catalyst surfaces, and surface reactions by mass spectrometry and low energy electron diffraction under ultra high vacuum.
- Modeled non-linear phenomena of oscillating surface reactions for improving selectivity between competing reactions.

1983-1985 **Norton Company, Worcester, MA.**
$1.2B worldwide manufacturer of ceramics, abrasives, and materials

- Powder processing, sintering, and characterization of non-oxide materials.
- Successful transfer of glass encapsulation hot isostatic pressing technology from Swedish company leading to a $7M new ceramic bearing business.

EDUCATION

1985-1990 **Ph.D. in Chemical Engineering**, University of California, Berkeley, CA.
Research Advisor: Alexis T. Bell. Experimental and modeling studies of adsorbate interactions with surfaces including adsorption, desorption, diffusion and reaction.

1979-1983 **B.S. Chemical Engineering**, Worcester Polytechnic Institute, Worcester, MA. Graduated with distinction. Exchange student to Zurich, Switzerland.

1979-1984

Fu-Hung Hsieh
Professor
Biological Engineering
Food Science
University of Missouri-Columbia

248 Agricultural Engineering Bldg.
Columbia, MO 65211-0001
TEL: (573) 882-2444
FAX: (573) 882=1115
E-mail: HsiehF@missouri.edu

Educational Experience:

B.S. 1969, Chemical Engineering, National Taiwan University
M.S. 1972, Chemical Engineering, Syracuse University
Ph.D. 1975, Food Science, University of Minnesota

Professional Experience:

Post-doctoral Fellow, Department of Chemical Engineering, University of Waterloo 1975-76
Research Associate, Chemical Engineering Section, Division of Chemistry, National Research Council Canada 1976-79
Research Scientist and Section Head, Grain Research Lab., Canadian Grain Commission, Agriculture Canada 1979-80
Manager and Research Engineer, Central Research Division, The Quaker Oats Company 1980-83
Senior Research Engineer, Technology and New Business Research, The Quaker Oats Company 1983-87
Faculty, Departments of Biological Engineering and Food Science, University of Missouri-Columbia 1987-present

Research:

Extrusion of food and feed. Viscoelastic, mechanical and thermal properties of biological materials. New uses of agricultural raw materials and by-products from food and feed industries. Biomaterials and biomechanics.

Teaching:

Principles of Biological Engineering II, Food Process Engineering I & II, Physical Principles of Food Processing, Food Extrusion, and Advanced Studies in the Science and Technology of Food Preservation.

Awards:

Gamma Sigma Delta Distinguished Award in Research, 1992.
Outstanding Teaching Professor in College of Engineering, 1994 and 1995.
Gold Chalk Award for Excellence in Graduate Teaching, 1995.
Chancellor's Award for Outstanding Faculty Research and Creative Activity in the Physical and Mathematical Sciences, 1998.
CAFS Professional Achievement Award, 2000.

LIST OF PUBLICATIONS:

1. Hsieh, F., Acott, K., Elizondo, H. and Labuza, T.P. 1975. The effect of water activity on the heat resistance of vegetative cells in the intermediate moisture range. Lebensm. Wiss. Technol., 8:78-81.
2. Hsieh, F., Acott, K. and Labuza, T.P. 1976. Death kinetics of pathogens in a pasta product. J. Food Sci., 41:516-519.
3. Hsieh, F., Acott, K. and Labuza, T.P. 1976. Prediction of microbial death during drying of a macaroni product. J. Milk Food Technol., 39:619-623.
4. Pamment, N., Moo-Young, M., Hsieh, F. and Robinson, C.W. 1978. Growth of *Chaetomium cellulolyticum* on alkali-pretreated hardwood sawdust solids and pretreatment liquor. Appl. Envir. Microbiol., 36:284-290.
5. Hsieh, F., Matsuura, T. and Sourirajan, S. 1979. Reverse osmosis separations of polyethylene glycols in dilute aqueous solutions using porous cellulose acetate membranes. J. Appl. Polym. Sci., 23:561-573.
6. Hsieh, F., Matsuura, T. and Sourirajan, S. 1979. Analysis of reverse osmosis data on polyethylene glycols-water-cellulose acetate membrane system at low operating pressures. Ind. Eng. Chem. Proc. Des. Dev., 18:414-423.
7. Hsieh, F., Matsuura, T. and Sourirajan, S. 1979. Analysis of reverse osmosis data for the system bovine serum albumin (BSA)-water-cellulose acetate membrane at low operating pressure. J. Separ. Proc. Technol., 1:50-61.
8. Sourirajan, S., Matsuura, T., Hsieh, F. and Gilbert, G.R. 1980. Production, specification and some transport characteristics of cellulose acetate ultrafiltration membranes for aqueous feed solutions. In : *Ultrafiltration Membranes and Applications*, Cooper, A. C., ed., Plenum, NY. pp. 21-43 .
9. Tweddle, T.A., Thayer, W.L., Matsuura, T., Hsieh, F. and Sourirajan, S. 1980. Specification of commercial reverse osmosis modules and predictability of their performance for water treatment applications. Desalination, 32:181-198.
10. Hsieh, F., Martin, D.G., Black, H.C. and Tipples, K.H. 1980. Some factors affecting the first break grinding of Canadian wheat. Cereal Chem., 57:217-223.
11. Black, H.C., Hsieh, F., Tipples, K.H. and Irvine, G.N. 1980. The GRL sifter for laboratory flour milling. Cereal Foods World, 25:757-760.
12. Black, H.C., Hsieh, F., Martin, D.G. and Tipples, K.H. 1980. Two Grain Research Laboratory mills and a comparison with the Allis-Chalmers mill. Cereal Chem., 57:402-406.
13. Hsieh, F., Daun, J.K. and Tipples, K.H. 1982. The effect of rapeseed oil added to control grain dust on the quality of wheat. J. Am. Oil Chem. Soc., 59:11-15.
14. Gould, M.R., Bone, D.P. and Hsieh, F. 1985. Cereal foods made from oats and methods of making. U.S. Patent 4,497,840.
15. Mulvaney, S.J. and Hsieh, F. 1988. Process control for extrusion operations. Cereal Foods World, 33:971-976.
16. Hsieh, F., Fields, M.L., Li, Y. and Huff, H.E. 1989. Ultra-high temperature effect on *Bacillus stearothermophilus* during puffing of rice. J. Food Qual., 12:345-354.
17. Hsieh, F., Huff, H.E., Peng, I.C. and Marek, S.W. 1989. Puffing of rice cakes as influenced by tempering and heating conditions. J. Food Sci., 54:1310-1312.
18. Hsieh, F., Mulvaney, S.J., Huff, H.E., Lue, S. and Brent, J. 1989. Effect of dietary fiber and screw speed on some extrusion processing and product variables. Lebensm. Wiss. Technol., 22:204-207.

19. Hsieh, F., Peng, I.C. and Huff, H.E. 1990. Effects of salt, sugar and screw speed on processing and product variables of corn meal extruded with a twin-screw extruder. J. Food Sci., 55:224-227.
20. Lue, S., Hsieh, F., Peng, I.C. and Huff, H.E. 1990. Expansion of corn extrudates containing dietary fiber: a microstructure study. Lebensm. Wiss. Technol., 23:165-173.
21. Hsieh, F., Young, L.S., Racicot, L.D., Raniwala, S.K. 1990. Process for infusing high levels of humectant into dried fruits, for use in dry foods, such as in mixes and ready to eat cereals. U.S. Patent No. 4,917,910.
22. Hsieh, F. 1990. Recent trends in food processing. In: *Proceedings of Modern Science and Technology Conference*, pp. 414-420, W.C. Chao, ed., Tunghai University, Taiwan.
23. Hsieh, F., Huff, H.E., Peng, I.C., Whittier, J.C., Schmitz, E.G. and Paterson, J.A. 1990. Studies of whole cottonseed extrusion with a twin-screw extruder. J. Food Eng., 12:293-306.
24. Hsieh, F., Hu, L., Peng, I.C. and Huff, H.E. 1990. Pretreating dent corn grits for puffing in a rice cake machine. J. Food Sci., 55:1345-1348, 1355.
25. Hsieh, F., Peng, I.C., Bailey, M.E., Clarke, A.D., Heymann, H. and Mulvaney, S.J. 1990. Restructuring of mechanically deboned meat by extrusion processing. In: *Engineering and Food*, Vol. 3, W.E.L. Spiess and H. Schubert, ed., Elsevier Applied Sci., London, pp. 378-384.
26. Hsieh, F., Hu, L., Huff, H.E. and Peng, I.C. 1990. Effects of water activity on textural characteristics of puffed rice cake. Lebensm. Wiss. Technol., 23:471-473.
27. Chao, R.R., Mulvaney, S.J., Sanson, D.R., Hsieh, F. and Tempesta, M.S. 1991. Supercritical CO_2 extraction of Annatto pigments and some characteristics of the color extracts. J. Food Sci., 56:80-83.
28. Hsieh, F., Peng, I.C., Clarke, A.D., Mulvaney, S.J. and Huff, H.E. 1991. Restructuring of mechanically deboned turkey by extrusion processing using cereal flours as a binder. Lebensm. Wiss. Technol., 24:139-144.
29. Hsieh, F., Young, L.S., Racicot, L.D., and Raniwala, S.K. 1991. Process for infusing high levels of humectant into dried fruits, for use in dry foods, such as in mixes and ready to eat cereals. U.S. Patent 5,000,971.
30. Lu, Q., Mulvaney, S.J. and Hsieh, F. 1991. Comparison of thermal processes for homogeneous and nonhomogeneous products in metal cans and retortable plastic containers. J. Food Sci., 56:835-837.
31. Hsieh, F. 1991. Extrusion and extrusion cooking. In : *Encyclopedia of Food Science and Technology*, pp. 794-800, Y.H. Hui, ed., Wiley-Interscience, New York, NY.
32. Hsieh, F. 1991. Ultrafiltration and reverse osmosis. In: *Encyclopedia of Food Science and Technology*, pp. 2614-2619, Y.H. Hui, ed., Wiley-Interscience, New York, NY.
33. Fair, N., Hsieh, F., Iannotti, E., Mueller, R., Neibling, H. and Tempesta. 1991. Environmental degradation of starch-filled polyethylene. INDA J. Nonwovens Res., 3:25-29.
34. Hsieh, F. and Luh, B.S. 1991. Breakfast rice cereals and baby foods. In: *Rice: Utilization*, 2nd ed., pp. 177-194, B.S. Luh, ed., Van Nostrand Reinhold, New York, NY.
35. Hsieh, F. and Luh, B.S. 1991. Rice snack foods. In: *Rice: Utilization*, 2nd ed., pp. 225-249, B.S. Luh, ed., Van Nostrand Reinhold, New York, NY.

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37. Hsieh, F., Huff, H.E., Lue, S. and Stringer, L. 1991. Twin-screw extrusion of sugar beet fiber and corn meal. Lebensm. Wiss. Technol., 24:495-500.
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39. Onwulata, C.I., Mulvaney, S.J., Hsieh, F. and Heymann, H. 1992. Influence of screw speed on process parameters and product quality of extruded corn meal. J. Food Sci., 57:512-515.
40. Lu, Q., Hsieh, F., Mulvaney, S.J., Tan, J. and Huff, H.E. 1992. Dynamic analysis of process variables for a twin screw extruder. Lebensm. Wiss. Technol., 25:261-270.
41. Huff, H.E., Hsieh, F., and Peng, I.C. 1992. Rice cake production using long-grain and medium-grain brown rice. J. Food Sci., 57:1164-1167.
42. Hsieh, F. 1992. Add values to agricultural raw materials through extrusion. In: *Agricultural Engineering and Rural Development*, Vol. I, pp. IV-1-3, W. Zhang et al., eds., International Academic Publishers, Beijing.
43. Flores, N.C., Clarke, A.D. and Hsieh, F. 1992. Extrusion processing of rice or corn flour with mechanically deboned turkey. J. Food Qual., 15:399-408.
44. Flores, N.C., Clarke, A.D., Heymann, H. and Hsieh, F. 1992. Sensory and textural characteristics of rice flour and mechanically deboned turkey extrudates. Lebensm. Wiss. Technol., 25:325-329.
45. Unklesbay, N., Unklesbay, K., Hsieh, F. and Sandik, K. 1992. Thermophysical properties of extruded beef/corn flour blends. J. Food Sci., 57:1282-1284.
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48. Hsieh, F., Grenus, K.M., Hu, L. and Huff, H.E. 1993. Twin-screw extrusion of rice flour with salt and sugar. Cereal Chem., 70:493-498.
49. Li, Y., Hsieh, F., Fields, M.L., Huff, H.E. and Badding, S.L. 1993. Thermal inactivation and injury of *Clostridium sporogenes* spores during extrusion of mechanically deboned turkey mixed with white corn flour. J. Food Proc. Pres., 17:391-403.
50. Bailey, M.E., Gutheil, R.A., Hsieh, F., Cheng, C., and Gerhardt, K.O. 1993. Maillard reaction volatile compounds and color quality of a whey protein concentrate-corn meal extruded product. In: *Thermally Generated Flavors*, pp. 315-327, T.H. Parliment, M.J. Morello, and R.J. McGorrin, ed., ACS Symposium Series No. 543, American Chemical Society, Washington, DC.
51. Hu, L., Hsieh, F. and Huff, H.E. 1993. Corn meal extrusion with emulsifier and soybean fiber. Lebensm. Wiss. Technol., 26:544-551.
52. Lue, S., Hsieh, F. and Huff, H.E. 1994. Modeling of twin-screw extrusion cooking of corn meal and sugar beet fiber mixtures. J. Food Eng., 21:263-289.
53. Onwulata, C.I., Mulvaney, S.J. and Hsieh, F. 1994. System analysis as the basis for control of density of extruded corn meal. Food Control, 5:39-48.

54. Jin, Z., Hsieh, F. and Huff, H.E. 1994. Extrusion cooking of corn meal with soy fiber, salt and sugar. Cereal Chem., 71:227-234.
55. Li, Y. and Hsieh, F. 1994. New melt conveying models for a single screw extruder. J. Food Proc. Eng., 17:299-324.
56. Peng, J., Huff, H.E. and Hsieh, F. 1994. An RTD determination method for extrusion cooking. J. Food Proc. Preserv., 18:263-277.
57. Liang, M., Hsieh, F., Huff, H.E. and Hu, L. 1994. Effects of barrel-valve assembly on twin-screw extrusion cooking of corn meal. J. Food Sci., 59:890-894.
58. Liang, M., Hsieh, F., Huff, H.E. and Hu, L. 1994. Barrel-valve assembly: Its influence on residence time distribution and flow pattern in a twin-screw extruder. Trans. ASAE., 37:1255-1261.
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60. Lin, Y., Huff, H.E., Parsons, M.H., Iannotti, E. and Hsieh, F. 1995. Mechanical properties of extruded high amylose starch for loose-filled packaging material. Lebensm. Wiss. Technol., 28:163-168.
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62. Hsieh, F., Young, L.S., Racicot, L.D., and Raniwala, S.K. 1991. Process for infusing high levels of humectant into dried fruits, for use in dry foods, such as in mixes and ready to eat cereals. Canadian Patent 1,334,258.
63. Badding-Smithey, S.L., Huff, H.E. and Hsieh, F. 1995. Processing parameters and product properties of extruded beef with nonmeat binders. Lebensm. Wiss. Technol., 28:386-394.
64. Jin, Z., Hsieh, F. and Huff, H.E. 1995. Physical properties and microstructure of corn meal extruded with soy fiber, salt and sugar. J. Cereal Sci., 22:185-194.
65. Huang, S., Liang, M., Huff, H.E., Kerley, M.S. and Hsieh, F. 1995. Extrusion cooking of rapeseed meal for reducing glucosinolates. Anim. Feed Sci. Technol., 56:1-9.
66. Hu, L., Huff, H.E., Heymann, H. and Hsieh, F. 1996. Effects of emulsifier and soy fiber addition on sensory properties of corn meal extrudate. J. Food Qual., 19:57-77.
67. Li, Y. and Hsieh, F. 1996. Modeling of flow in a single screw extruder. J. Food Eng., 27:353-375.
68. Lin, Y., Hsieh, F. Huff, H.E. and Iannotti, E. 1996. Physical, mechanical and thermal properties of water-blown rigid polyurethane foam containing soybean protein isolate. Cereal Chem., 73:189-196.
69. Parsons, M.H., Hsieh, F. and Huff, H.E. 1996. Extrusion cooking of corn meal with sodium bicarbonate and sodium aluminum phosphate. J. Food Proc. Preserv., 20:221-234.
70. Tan, J., Chang, Z. and Hsieh, F. 1996. Implementation of an automated real-time statistical process controller. J. Food Proc. Eng., 19:49-61.
71. Li, Y., Lu, Q., Huff, H.E. and Hsieh, F. 1996. On-line measurements of rheological properties of corn meal using a co-rotating self-wiping twin-screw extruder. Trans. Inst. Chem. Eng., Part C - Food and Bioprod. Proc., 74:149-158.
72. Lin, Y. and Hsieh, F. 1996. Measurement and prediction of apparent thermal conductivity of plastic foam with or without biomass materials. Appl. Mech. Eng., 1:465-480.
73. Li, Y., Huff, H.E. and Hsieh, F. 1996. Flow modeling of a power-law fluid in a fully wiped, co-rotating twin-screw extruder. J. Food Proc. Eng., 20:141-163.

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93. Hsieh, F. 1999. Ultrafiltration. In: *Wiley Encyclopedia of Food Science and Technology*, Vol. 4, pp. 2357-2362, Frederick J. Francis, ed., John Wiley & Sons, New York, NY.
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95. Tang, C., Heymann, H. and Hsieh, F. 2000. Alternatives to data averaging of consumer preference data. Food Quality and Preference 11:99-104.
96. Lin, S., Hsieh, F. and Huff, H.E. 2000. Texture and chemical characteristics of high moisture soy protein meat analog. J. Food Sci., 65:264-269.
97. Liu, Y., Hsieh, F., Heymann, H. and Huff, H.E. 2000. Effect of process conditions on the physical properties of extruded oat-corn puff. J. Food Sci., 65:1253-1259.
98. Rolfe, L.A., Huff, H.E. and Hsieh, F. 2000. The effect of processing conditions on the quality of an extruded catfish feed. Trans. ASAE, 43(6):1737-1743.
99. Chang, L., Xue, Y. and Hsieh, F. 2001. Comparative study of physical properties of water-blown rigid polyurethane foams extended with commercial soy flour. J. Appl. Polym. Sci., 80(1):10-19.
100. Rolfe, L.A., Huff, H.E. and Hsieh, F. 2001. Effects of particle size and processing variables on the properties of an extruded catfish feed. J. Aquatic Food Product Technol., in press.
101. Chang, L., Xue, Y. and Hsieh, F. 2001. Dynamic-mechanical study of water-blown rigid polyurethane foams with and without soy flour. J. Appl. Polym. Sci., in press.
102. Lin, S., H. E. Huff and F. Hsieh. 2001. Extruder responses, sensory characteristics, and structural properties of high moisture soy protein meat analog. J. Food Sci., in press.

CURRICULUM VITAE

TROY NORRED
4511 ROYAL LYTHAM DR
COLUMBIA MO 65203
573-443-8301
email – norred99@aol.com

PERSONAL:

BIRTHDATE: NOV. 28 1967
NORMAN OKLAHOMA

SPOUSE: LAURA NORRED
DEPENDENTS: TROY M. NORRED
SARAH E. NORRED
TRISTAN A. NORRED
TRENTON D. NORRED

EDUCATIONAL:

MEDICAL SCHOOL: UNIVERSITY OF OKLAHOMA COLLEGE OF MEDICINE

1990-1995 GRAD. MD.

COLLEGE: EAST CENTRAL OK. UNIV.
ADA, OK. 1986 - 1990
BS BIOLOGY/PHYSICS

HIGH SCHOOL: ASHER HIGH SCHOOL
ASHER, OK. 1982 - 1986
DIPLOMA

RESEARCH EXPERIENCE:

OCT. 1991 - AUG 1992 DEPT OF UROLOGY
MOLECULAR BIOLOGY
RESPONSIBILITIES: I HAD THE PRIMARY RESPONSIBILITY OF THE DESIGN, IMPLIMENTATION, AND INTERPRETATION OF THE EXPERIMENTS. I ALSO WROTE AND SUBMITTED THE ARTICLE FOR PUBLICATION IN CONCERT WITH DR. ROBERT HURST.

MAY 1991 - AUG 1991 DEPT. OF INTERN. MED.
MOLECULAR BIOLOGY
RESPONSIBILITIES: I HELPED START A LAB WITH DR. TOM CARTER WHO HAD RECENTLY ACCEPTED THE APPOINTMENT. HIS INTEREST INCLUDED THE ONCOGENE ERB B AND ITS COMPLETE CHARACTERIZATION.

MAY 1990 - AUG 1990 DEPT OF ANATOMICAL
SCIENCES.
NEURAL CORTICAL STIMULATION
I DESIGNED A FEEDING APPARATUS, WHICH WOULD ALLOW FOR THE DORSIFLEXION OF A RAT THUMB. WE THEN MAPPED THE INFLUENCE THIS HAD ON THE REPRESENTATION IN THE PARIETAL CORTEX.

MAY 1987 - DEC 1989 ROBERT S. KERR ENVIRONMENTAL RESEARCH
LABORATORY
ENVIRONMENTAL RESEARCH
MOLECULAR BIOLOGY
THIS WAS MY FIRST EXPERIENCE IN MOLECULAR BIOLOGY AND ITS TOOLS IN RESEARCH. I BEGAN WASHING DISHES AND ENDED SETTING UP NITROGEN BASED EXPERIMENTS FOR THE ENHANCED DEGRADATION OF HYDROCARBONS IN JET FUEL SPILLS. THIS WAS A TREMENDOUS EXPERIENCE FOR ME.

PUBLICATIONS:

ANNALS OF BIOCHEMISTRY -SUBTRACTIVE HYBRID-IZATION FOR SELECTION OF RARELY EXPRESSED GENES. 1992. (COPIES AVAILABLE UPON REQUEST)

PATENTS

AQUATREADMILL EQUINE COPATENT
AQUATREADMILL HOMOSAPIEN COPATENT
SIEVING SYSTEM FOR HIGH QUALITY SILICONE PROPRIETARY PATENT
PERCUTANEOUS AORTIC VALVE SYSTEM

MEDICAL SCHOOL ACTIVITIES:

AIDS AWARENESS AMONG HIGH SCHOOL STUDENTS
INFANT IMMUNIZATION AWARENESS
MARY MAHONEY VOLUNTEER CLINIC

COMMUNITY ACTIVITIES:

VOLUNTEER TUTOR E.K. GAYLORD WOMEN'S CRISIS CENTER
TUTOR AT NE HIGH SCHOOL OKLAHOMA CITY
MISSION WORK IN GUATAMALA

UNDERGRADUATE HONORS/ACTIVITIES

ALPHA CHI HONOR SOCIETY - VICE PRESIDENT
OUTSTANDING SENIOR BIOLOGY MAJOR
VICE PRESIDENT OF YOUNG DEMOCRATS
STATE PARLIMENTARIAN OF THE YOUNG DEMOCRATS
OUTSTANDING FRESHMAN IN SCIENCES AWARD
PRESIDENT PHYSICS CLUB
PUTNAM MATH COMPETION

WORK EXPERIENCE

1. FELLOWSHIP — JULY 1998 TO PRESENT
UNIVERSITY HOSPITAL
UNIVERSITY OF MISSOURI
ONE HOSPITAL DRIVE
COLUMBIA, MO. 65203

PROCEDURAL EXPERIENCE:

1. CORONARY ANGIOGRAMS TO DATE #340 (AS OF 8/10/00)
2. RIGHT HEART CATHETERIZATIONS #150
3. TRANSESOPHAGEAL ECHOCARDIOGRAM #72
4. STRESS ECHOCARDIOGRAMS #250
5. NUCLEAR STRESS SESTAMIBI #350
6. RIGHT HEART BIOPSIES #140

1. RESIDENCY — JULY 1996 TO 1998
UNIVERSITY HOSPITAL
OUHSC
OKC.OK.

2. INTERNSHIP — JULY 1995 -JULY 1996
UNIVERSITY HOSPITAL
OUHSC

OKC. OK.
HOWELL SCOFFIELD AWARD

3.DEPT OF UROLOGY
Associate Research Professor
OUHSC 1991 - 1992
940 STANTON L YOUNG BLVD
OKC OK. 73104

4. PREVIOUSLY MENTIONED RESEARCH EXPERIENCE

PROFESSIONAL MEMBERSHIPS:

ACC
OSMA
AMA

REFERENCES:

1. TIMOTHY CATCHINGS MD
   ASSOCIATE PROFESSOR
   UNIVERSITY OF MISSOURI
   ONE HOSPITAL DRIVE
   COLUMBIA MO 65203
   573-882-7272
2. DARLA HESS MD
   ASSOCIATE PROFESSOR
   UNIVERSITY OF MISSOURI
   ONE HOSPITAL DRIVE
   COLUMBIA MO 65203
   573-882-7272
3. H K REDDY MD
   ASSOCIATE PROFESSOR
   UNIVERSITY OF MISSOURI
   ONE HOSPITAL DRIVE
   COLUMBIA MO 65203
   573-882-7272
4. DOUGLAS FINE MD
   CHAIRMAN DEPARTMENT OF INTERNAL MEDICINE
   UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
   940 STANTON L YOUNG BLVD
   OKLAHOMA CITY, OKLAHOMA 73102
   405-271-5656
5. SYLVIA BOTTOMLEY MD
   PROFESSOR OF MEDICINE
   UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
   940 STANTON L YOUNG BLVD
   OKLAHOMA CITY, OKLAHOMA 73102
   405-271-5656
6. DR. EBSTEIN MD

UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
940 STANTON L YOUNG BLVD
OKLAHOMA CITY, OKLAHOMA 73102

PROFESSOR OF MEDICINE

405-271-5656

7. DR ROBERT HURST PhD
PROFESSOR BIOCHEMISTRY AND UROLOGY
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
940 STANTON L YOUNG BLVD
OKLAHOMA CITY, OKLAHOMA 73102

BIBLIOGRAPHY