Suggs

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MEMORANDUM

To: Director of Research

Date: March 4, 1977

From: F. J. Hassler (Name and Signature) Head of: Biological and Agricultural Engineering

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Title: A Study of Mechanical Properties of Mammary Tissue With Emphasis on Driving Point Mechanical Impedance as a Tumor Diagnostic Technique

Author(s) S. W. Glass and C. W. Suggs

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Journal of **BIOMECHANICS**

12 May 1978

S.W. Glass
Dept. Biological and Agricultural Engr.
N.C. State Univ.
Raleigh, NC

Dear Dr. Glass:

I regret to inform you that your revised manuscript is still weak in the opinion of our reviewers. Please find his comments enclosed. Perhaps you could take his suggestions and shorten the paper to the lenght of a technical note, otherwise we will be unable to publish the paper in its present form.

I am sorry that I must take this action and hope that you will continue to consider the journal as a suitable publication source.

Sincerely,

VLR

Verne L. Roberts Ph.D.
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Journal of BIOMECHANICS

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REFEREE REPORT 77-219 REV. I

TITLE: MECHANICAL PROPERTIES OF MAMMARY TISSUE WITH EMPHASIS ON DRIVING POINT MECHANICAL IMPEDANCE

AUTHOR: GLASS AND SUGGS

Referee Decision

- ACCEPT ☐
- RETURN FOR REVISION ☐
- REJECT - UNSUITABLE ☐

Referee Comments:

The paper is still weak in that the length of the paper is too long for the results obtained and the results are mostly negative. What is the value of reporting the work with foam rubber if its purpose was to develop the testing techniques and does not contribute directly to the major objective?

My suggestion would be to emphasize the positive aspects of the work (development of a six-element model) and greatly reduce the space devoted to the other aspects.

Date: ____________________ Signed: ____________________

PLEASE RETURN SIGNED ORIGINAL AND UNSIGNED CARBONS

Jan 8-78
Revised

Mechanical Properties of Mammary Tissue With Emphasis on Driving Point Mechanical Impedance[1/]

S.W. Glass and C.W. Suggs[2/]
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N.C. State University
Raleigh, N.C.

ABSTRACT

Quasistatic compression tests, free vibration tests and driving point mechanical impedance tests were performed on foam rubber, *in vitro* cow udder and *in vivo* human mammary tissue. In the quasistatic test, serous carcinoma tumor tissue was found to have a compression modulus over three times that of normal breast tissue. In the free vibration test, the transient response of tissue to an impulse revealed that stiffness was directly related to preload on the tissue while the natural frequency and damping ratio remained constant. Driving point mechanical impedance tests on foam rubber, *in vitro*, and *in vivo* mammary tissue showed impedance to be primarily a function of tissue thickness. Lumps of steel and wood were inserted into foam rubber with a dramatic difference between 'with lump' and 'without lump' conditions. Similar *in vitro* cow udder tests showed only a small difference with the steel lump. No distinction between cystic breast lumps and normal tissue could be made. A six element lumped parameter model was fit to the observed data. It was found that the same model with slightly altered parameters fit both 'with lump' and 'without lump' systems. Based on these results, lumps of similar specific gravity to that of the surrounding soft tissue seem to vibrate with that surrounding tissue such that they are unsuitable for detection by mechanical impedance techniques.

[1/] Paper number 5226 of the journal series of the North Carolina Agricultural Experiment Station, Raleigh, N.C. The use of trade names in this publication does not imply endorsement by the North Carolina Agricultural Experiment Station of the products mentioned nor criticism of similar ones not mentioned.

[2/] Graduate Assistant and Professor, Department of Biological and Agricultural Engineering. North Carolina State University, Raleigh, N.C.

There is evidence, however, to suggest further in vivo investigation in the region above 1000 Hz and below 30 Hz, along with more modeling and clinical tests.

INTRODUCTION

In this study, certain mammary tissue mechanical properties, particularly those believed to have clinical diagnostic potential were investigated. Three types of tests were performed, quasistatic stress-strain, free vibration and driving point mechanical impedance.

Yamada (1969) has collected a comprehensive anthology of quasistatic test results. In his study of scalp and brain tissue McElhaney (1972) also used free vibration tests and forced vibration tests similar to those used in this investigation. Suggs and Abrams (1971) emphasized driving point mechanical impedance measurement technique and the merits of lumped parameter and continuous modeling techniques in describing the nature of the biological materials. The importance of driving point mechanical impedance as a diagnostic technique has been investigated by Thompson (1973) and Entrekin (1975) in connection with the fracture and healing of the human ulnar.

QUASISTATIC UNIAXIAL COMPRESSIVE STRAIN TEST

Method

An Instron universal testing machine with a 1 inch diameter compressing piston (considerably smaller than the sample size) was used. Samples were all prepared in the same way. A region of interest was dissected from the specimen, then a flat slab was sliced off with a minimum width of 5.0 cm and a thickness ranging from 0.5 to 3.0 cm. Tissues tested were normal and pathological cow mammary tissue and human mastectomy tissue.

Some of the cow udder tissue samples were tested immediately after removal from the animal. Others were immersed in formalin for 15 to 20 minutes then stored dry in closed containers at room temperature overnight. This procedure simulated the history of human tissue after surgical removal and thus demonstrated the effect of the preservative.

Results and Discussion

Although a tendency for the formalin fixed udder tissue to be stiffer was noted, an f test at the 95% level showed no significant difference. Results from the fixed human tissue therefore may be assumed representative of fresh unfixed tissue. Only four carcinoma samples were tested due to the difficulty in acquiring samples. Although the variation was large, the mean slope of the stress-strain curve of the serous carcinoma tissue is over three times as great as that of normal breast stroma (Fig. 1). In order to better evaluate differences, a secant modulus estimate at 15% strain for the compression modulus was computed for each curve. Coefficients of variation and LSD values were calculated. No significant difference as a result of the formalin treatment or between fixed breast and unfixed udder stroma was found (Table 1). There was, however, a difference among breast carcinoma, bovine supramammary lumph node tissue, mastitic scar tissue, skin, and mammary stroma tissue.

A mechanical test sensitive to material stiffness may therefore be a potentially valuable diagnostic aid. Although quasistatic stress strain tests are limited to excized tissues, perhaps other techniques can be made sensitive to different stiffnesses within tissues as a non-invasive method.

FREE VIBRATION TEST

Method

By observing the decaying vibration of a material in response to a step input, the natural frequency, ω_n, damping ratio, ζ, and stiffness, k, may be estimated.

QUASISTATIC COMPRESSION STRESS - STRAIN
PLOTS OF NORMAL AND PATHOLOGICAL TISSUE

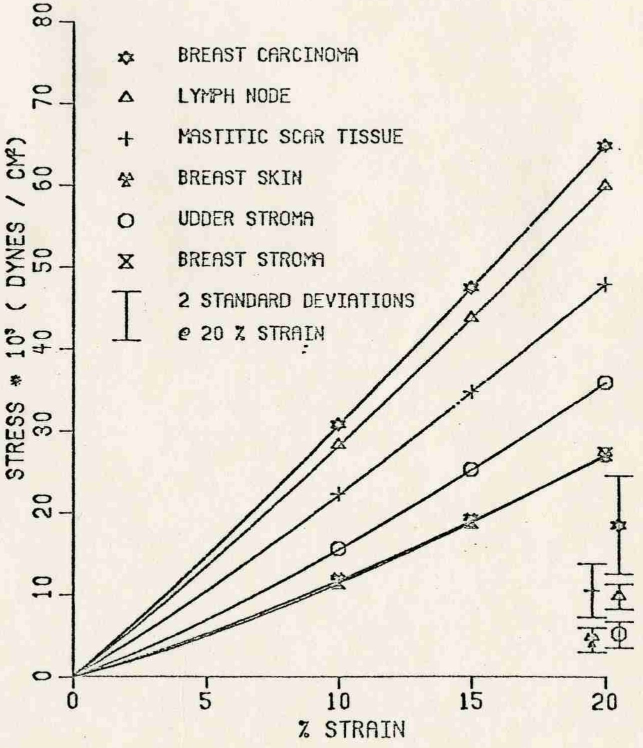

Figure 1. Test results for normal and pathological tissue

Table 1. Modulus of Compression of Various Tissue Samples.

Tissue Sample Type	Number of Observations	Number of Subjects	Modulus of x 10^3 Compression (dynes/cm^2)	Significant Difference @ .05 (LSD=14.1)	Standard Deviation	% Coefficient of Variance
Breast Carcinoma	4	4	340		60.6	17.8
Foam Rubber	5	1	261	yes	3.1	.011
Lymph Node	12	3	229	yes	25.1	10.9
Mastitic Scar Tissue	20	5	196	yes	18.2	9.3
Udder Skin (Fixed)	16	4	150	yes	10.3	6.9
Human Skin (Fixed)	4	4	141	no	19.6	13.9
Udder Skin (Unfixed)	20	5	139		8.6	6.2
Udder Tissue (Fixed)	16	4	106	yes	14.7	13.9
Udder Tissue (Unfixed)	20	5	102	no	14.2	14.0
Breast Stroma	9	4	89	no	13.8	15.5

Since the object of this test was only to provide a general understanding of the dynamic behavior of soft tissue, only cow udder tissue was tested.

Flat slabs of tissue 1 cm thick were prepared as in the quasistatic test and placed between horizontal 3.8 cm diameter plattens. The lower platten was connected to a piezoelectric force gage while the upper platten was loaded with incrementing masses from 0.1 to 0.5 kilograms. The mass was then tapped with a steel striker resulting in a decaying sinusoidal signal from the force transducer to a storage oscilloscope. For linear materials the amplitude of the step input is inconsequential since only ratios of deck magnitudes are used in the calculations. Although mammary tissue is clearly not linear as seen in the quasistatic response and the driving point mechanical impedance plots, linearity seems an acceptable assumption for the free vibration study. The damping ratio, ζ, was found by the logarithmic decrement method.

Results and Discussion

Of the five udder stroma tissues sampled, the damping ratio was found to be fairly constant as the mass resting on top of the material was varied (Fig. 2a). The mean damping ratio was .0902 with a coefficient of variance of .6%. The natural frequency was also fairly constant, however, stiffness was found to increase linearly with increased mass (Figure 2b and 2c). Such behavior is in contrast to the more typical fixed stiffness and decreasing natural frequency as a function of increasing mass for the classical network representation of mechanical systems. This type of behavior might be anticipated however from the nonlinear stress-strain response. When the strain level was low (small mass) the slope, i.e., stiffness, was lower than for higher strain levels (large mass). This also indicates that the static preload will have a dramatic effect on the dynamic impedance plots.

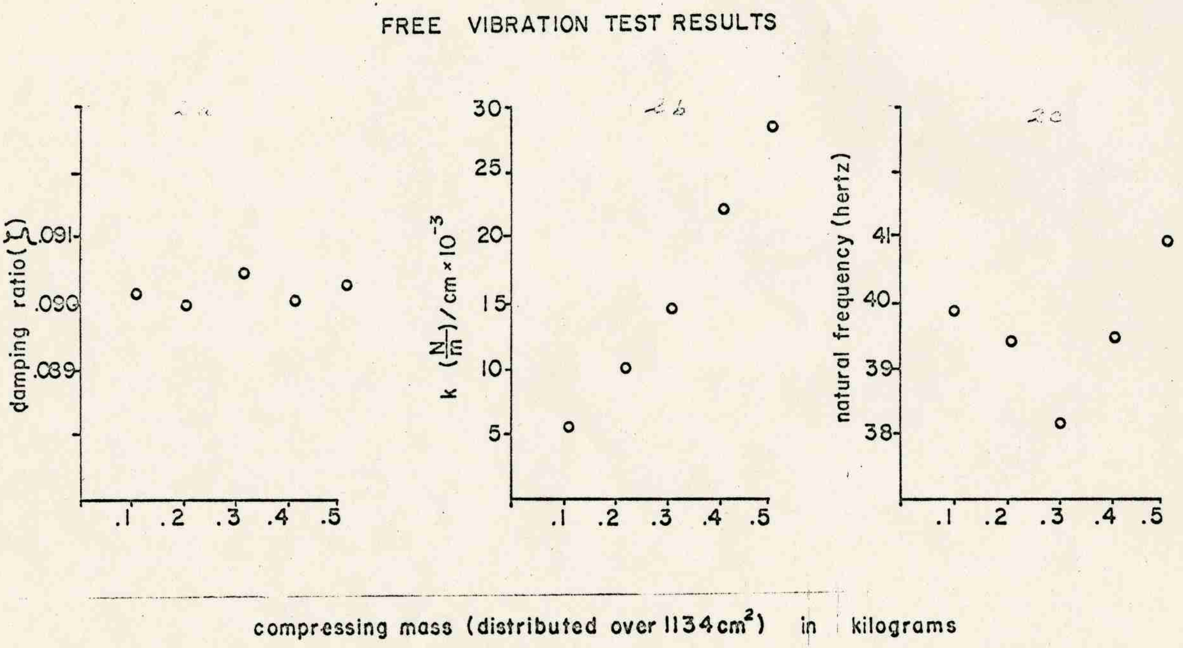

Figure 2 Free vibration test results: spring constant, k; natural frequency, f_n; and damping ratio, ζ; all shown as a function of loading mass

DRIVING POINT MECHANICAL IMPEDANCE TEST

Introduction

Driving point mechanical impedance is a complex quantity describing the ratio of the force of excitation to the resulting velocity of the system. By expressing the frequency response of impedance in polar form, it is possible to represent a continuous frequency spectrum by two, two dimensional plots, i.e. impedance magnitude versus frequency and phase angle (force with respect to velocity) versus frequency. Conveniently, this kind of representation has a family of pure mass contours with a magnitude slope of +20 db per decade and a $+90^{\circ}$ phase angle, pure spring contours with a magnitude slope of -20 db per decade and -90° phase angle and pure damping with 0 magnitude slope and 0° phase angle. This helps in modeling the response and ultimately relating the impedance plots back to the biological system.

Method

A continuous sweep, automatic computing and recording impedance measuring system was used. In response to the movement of the shaker, the A.C. force and acceleration signals from the impedance head are passed to the mass cancellation amplifier. By taking advantage of Newton's second law, the acceleration signal (which is in phase with the force signal for a pure mass) may be used to subtract the effect of the mass of the interface fixture from the total force signal. The result is a force signal of the sample object alone. After passing through a tracking filter to eliminate any nonlinear distortion, the mechanical impedance, both magnitude and phase angle, are computed and recorded on both a real time x, y, y′ plotter and on a multichannel FM tape recorder. The taped data was later digitized and stored on disks for statistical analysis and computer plotting. (Spectral Dynamics, 1974).

The shaker, resting on top of the test sample was hand steadied, Figure 3.

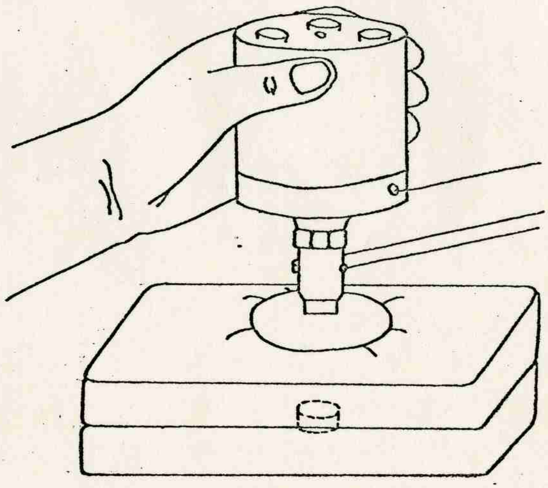

Figure 3. Test arrangement for foam rubber lump test

At first the static preload per unit of interface area was controlled by changing the size of the interface. Later, however, a system of counterweights was added for more precise control of the preload. For most samples, both the 20 cm^2 and the 5 cm^2 interface areas were tried. The larger interface area was less subject to local variations in mechanical properties of the foam rubber and the cow udder material however it could not adequately interface the human breast tissue due to the natural curvature of the surface. The smaller interface area showed more dramatic differences between the with lump and without lump conditions. Although static preload and interface area have a pronounced effect on the impedance magnitude, the general shape of the frequency response plot is relatively unaltered.

The acceleration level in all tests was 0.5 g (4.9 m/s^2) and the frequency range was from 30 to 1000 Hz. The upper frequency limit was guided by Mishoe (1974) and others who suggest that near surface properties dominate the response with increased frequency. The lower limit was due to limitations of the excitor system.

Because of its similar quasistatic stiffness to mammary tissue and because it was more convenient to use than animal tissue, foam rubber was used to develop most of the dynamic testing techniques. Except for its very low damping, foam rubber's dynamic characteristics were also similar to animal tissue. Absence of the smoothing effect of damping on the frequency profile provided a better opportunity for observation and modeling of soft material vibration behavior. These observations and models were then transferred and tested on the more subtle curves of the animal tissue.

A small cylindrical lump (diameter 1.27 cm, height 0.635 cm), one of wood and one of steel weighing 0.8 and 8 grams respectively, was inserted into the foam rubber and the cow udder material. The lump's characteristics differed from their surrounding medium far more than would a carcinoma and therefore should be easier to diagnose. Had the animal lump tests been more conclusive, lumps which better resemble the carcinomas could have been tested.

Where it was possible and appropriate, a number of impedance plots were reduced to a single mean plot. In order to be absolutely correct, the mean value of several complex numbers must be computed from their rectangular forms at each frequency. For small differences in the phase angle however, the error introduced by computing means of each polar co-ordinate was less than 5%. Consequently this method was used.

In an attempt to reduce a group of plots to a single valued indication of variance, the mean coefficient of variance, ($\% \overline{C.V.}$), was used. An average coefficient of variance was calculated from magnitude and phase at each frequency. Note that log values are used for the magnitude computations and the phase angles are offset by 90^{o} in order to eliminate division by zero.

$$\% \overline{C.V.} = \frac{100 \times \sum_{i=1}^{n} \left(\frac{\log (\sigma_z)_i}{\log (Z)_i} + \frac{(\sigma_\phi)_i}{(\phi_i + 90^{o})} \right)}{n} \qquad \text{Eq. 4}$$

In Equation 4, σ is the standard deviation and $\overline{Z}$ and $\overline{\phi}$ are the mean impedance magnitude and phase angle respectively.

Results and Discussion

Foam Rubber Test

It was found that the sample thickness had a pronounced effect on the impedance response. Increments of 2.54 cm from 2.54 cm to 7.62 cm were tested. With increased sample thickness, the primary resonance dropped from 600 Hz to 90 Hz, constant stiffness asymptopes were lowered, constant mass asymptotes below 500 Hz were raised, however constant mass asymptotes above 700 Hz were changed very little. This supports the claim that higher frequency response is primarily influenced by the near surface region.

In the foam rubber lump test, a dramatic difference between the impedance plots of foam rubber with and without a steel lump was noted. The wooden lump's plot was also distinguishable from that of the 'no lump' use although not nearly to the same extent, Figure 4. This implies that at least part of the lump's altered impedance resonance is related to the mass of the lump relative to the mass of the surrounding tissue. The specific gravity of the compressed foam was estimated at 0.35 compared to 0.87 for wood and over 7.0 for steel. Carcinoma tumor tissue's specific gravity however is within 10% of the surrounding stroma and therefore is not likely to be detectable if the technique is only sensitive to specific gravity differences.

In Vitro Cow Udder Tests

In vitro cow udder tissue was also tested in much the same manner as was the foam rubber. Tissue was refrigerated immediately after necropsy then warmed to body temperature for testing. Less than 24 hours elapsed between death and the tissue test.

The first series of experiments involved measurements at several well defined anatomical locations on an intact udder. A considerable variation was found between both different anatomical locations on a single udder and between similar anatomical locations on different udders. As in the foam rubber, the most important factor in determining the mechanical impedance was the tissue thickness. In order to best show this, cow udder tissue was frozen then sawed into 1 cm incrementing thickness slabs, thawed, warmed and tested, Fig. 5.

In order to show the effect of freezing the tissue, ten samples were marked then tested both before and after the freeze procedure. An F test at the 5% level ($\alpha = 0.95$) showed no significant difference between the two classes of curves.

Lump tests were also performed on the in vitro udder tissue. Unlike the foam rubber however, three plots were made for each sample, one for the 'no lump' condition,

FOAM RUBBER LUMP TEST

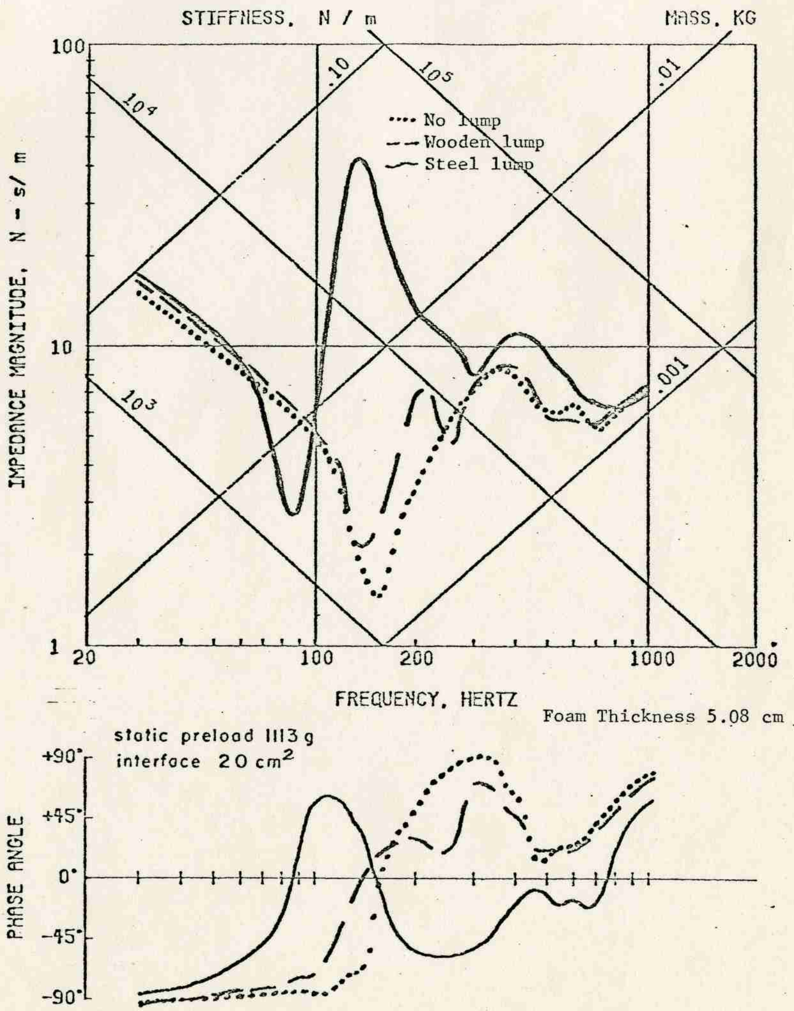

Figure 4. Foam rubber lump test for 8 g cylindrical steel lump and 1 g cylindrical wooden lump

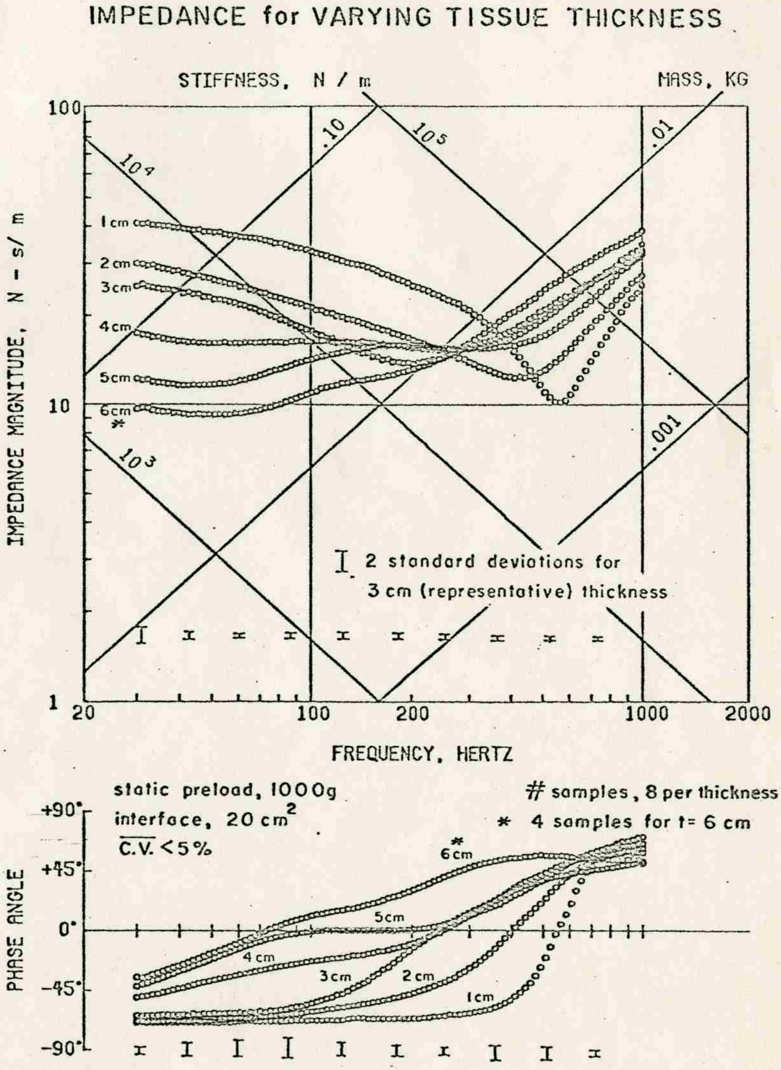

Figure 5. Means from sawed cow udder tissue for six different thicknesses of tissue

a second for the tissue sample after an incision or 'slit' was made but before the insertion of the lump, and a third with the lump inserted into the slit. The slit was made perpendicular to the direction of vibration because it was found that this direction produced the least distorting results. Very little difference was found between the no lump condition and the light wooden lump test in the magnitude curve. The phase line, however, is distinctly different above 400 Hz for the two cm thick tissue sample, Fig. 6. The steepness of the slope at 1000 Hz indicates an additional high frequency resonance.

Since differences between 'with lump' and 'without lump' impedances would be most prominant at some condition of resonance, further investigation above 1000 Hz may be worthwhile. The region below 30 Hz also may show differences since the primary resonances for the thicker udder tissues and all of the human tests seem to be below 30 Hz.

For all tissue thicknesses up to six cm, a trend of greater inflection in the steel lump plot than in the no lump plot may be noted, Fig. 7. The differences, however, are more pronounced in the thinner tissue samples. Increased degree of inflection seems the most consistent and detectable indication of a lump. Furthermore, since the degree of inflection seems related to the mass of the lump and the tissue thickness, detection of stiffness differences within the tissue is doubtful.

In Vivo Breast Tissue Test

Seven women of varying breast size, ranging in age from 21 to 31 years of age were tested. Subjects were asked to lie on their back or side such that the tangent to their ribcage at the point of excitation was parallel with the table and perpendicular to the shaking axis. Four points were tested on each breast, located above, below, medially and laterally from the nipple at a distance of three centimeters. In addition, if the subject knew of any cystic lumps, they were located and tested along with the bilaterally symetrical position.

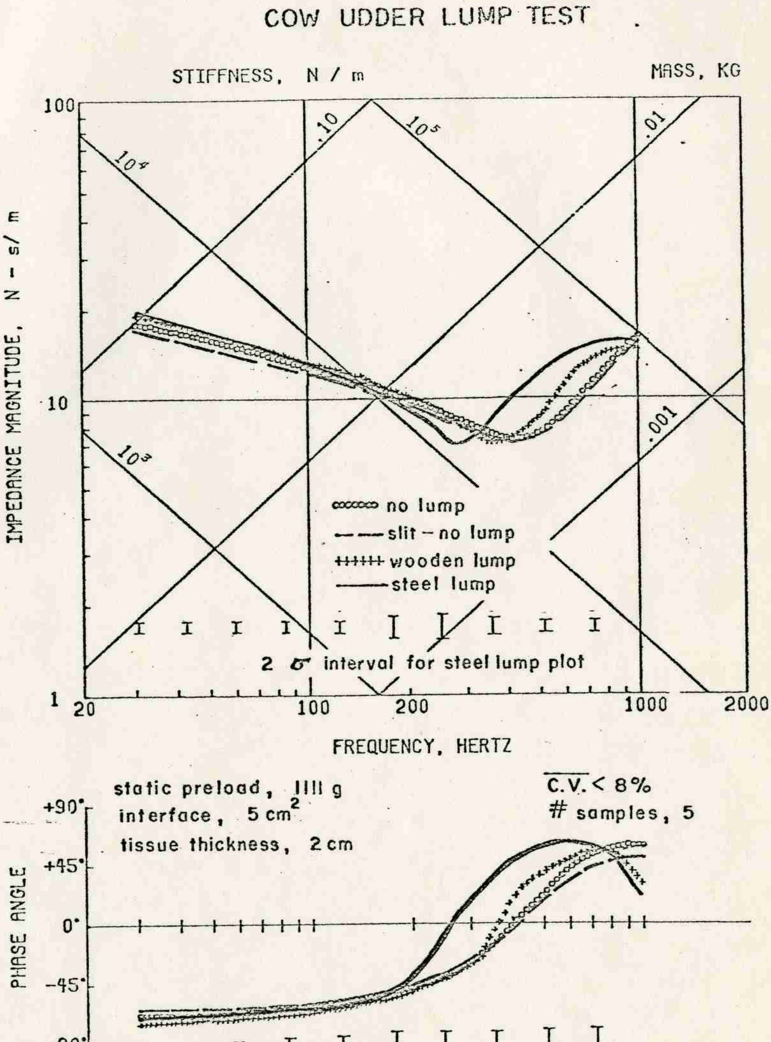

Figure 6. Means from 5 lump tests on 2 cm thick tissue for steel and wooden lumps weighing 8 and 1 g, respectively

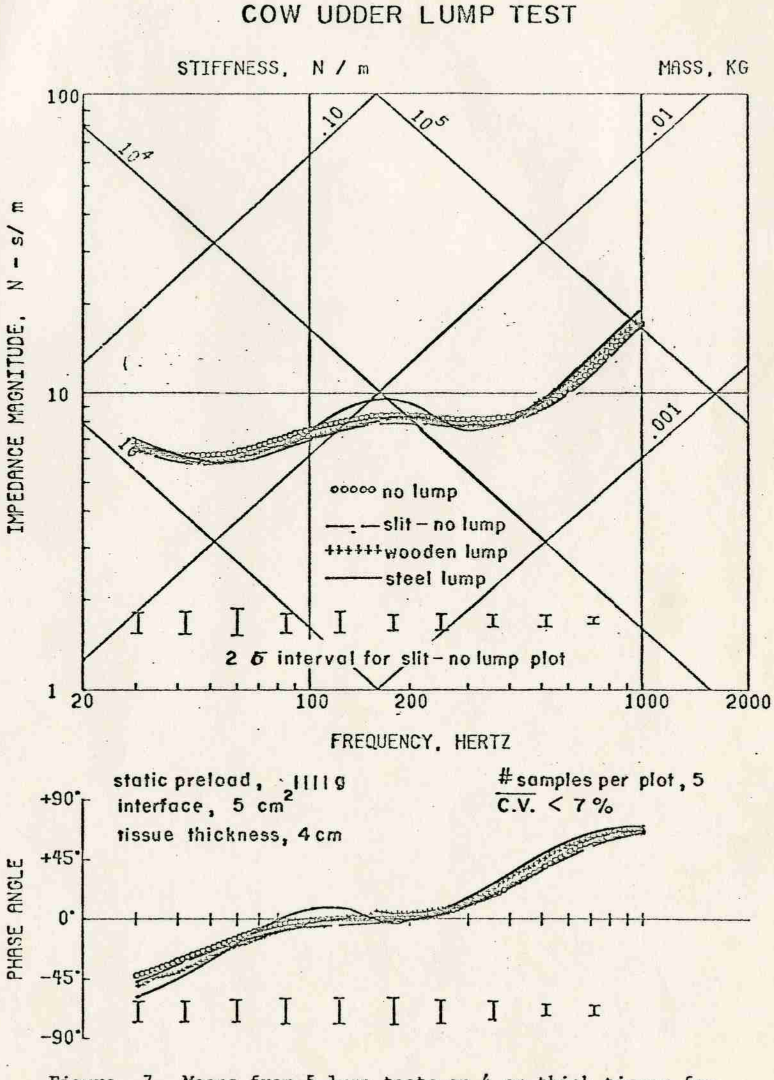

Figure 7. Means from 5 lump tests on 4 cm thick tissue for steel and wooden lumps weighing 8 and 1 g, respectively

Although *in vivo* tissue thickness could only be estimated, the sample thickness was found to be the most important factor in determining the nature of the impedance plot. As tissue thickness increased, however, the *in vivo* tissue showed a different response from that noted in the cow udder tissue. In the cow tissue, with increasing tissue thickness, the impedance magnitude for the lower frequencies (below 200 Hz) decreased. In human tissue, the plots for thicker samples tend to have less inflection and higher impedance magnitude values, Figure 8. An earlier set of experiments on goat udders, *in vivo*, showed the same effect. This may represent the differences associated with the higher concentration of fluid in the *in vivo* versus the *in vitro* state.

Figure 9 shows two lump tests for women reporting cystic lumps. The lower magnitude curve shows the most difference between the lump condition and the no lump condition. Although the actual impedance values are very nearly the same, and there are no apparent additional resonances or antiresonances, in the lump plot, the lump curve shape has somewhat pronounced inflections and therefore indicates the presence of lumps. The upper curves, however, are more typical of the lump test results among women reporting cystic lumps. No significant difference was noted at any frequency for either of the lump tests. Driving point mechanical impedance must then be considered an unpromising mammary lump detecting technique in this frequency range. Due to the one positive test, clinical trials on women with confirmed carcinomas should be considered.

A LUMPED PARAMETER MODEL FOR MAMMARY TISSUE

Unless impedance plots like those already shown can be related to the physical characteristics of the tissue and then normalized for certain sets of conditions, they are of limited use in understanding the behavior of a tissue system. By trial and error it was found that the transfer function describing the six element mechanical network of Figure 10 also generally conforms to the observed mechanical

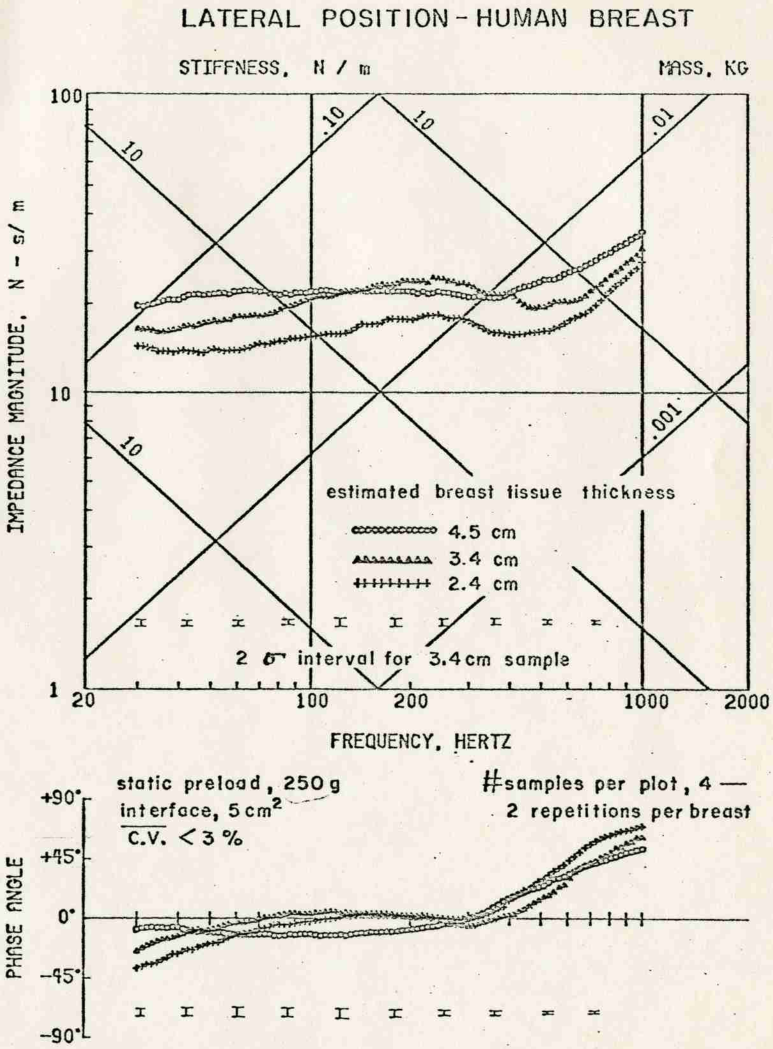

Figure 8. Lateral test position from large, medium and small breasted women

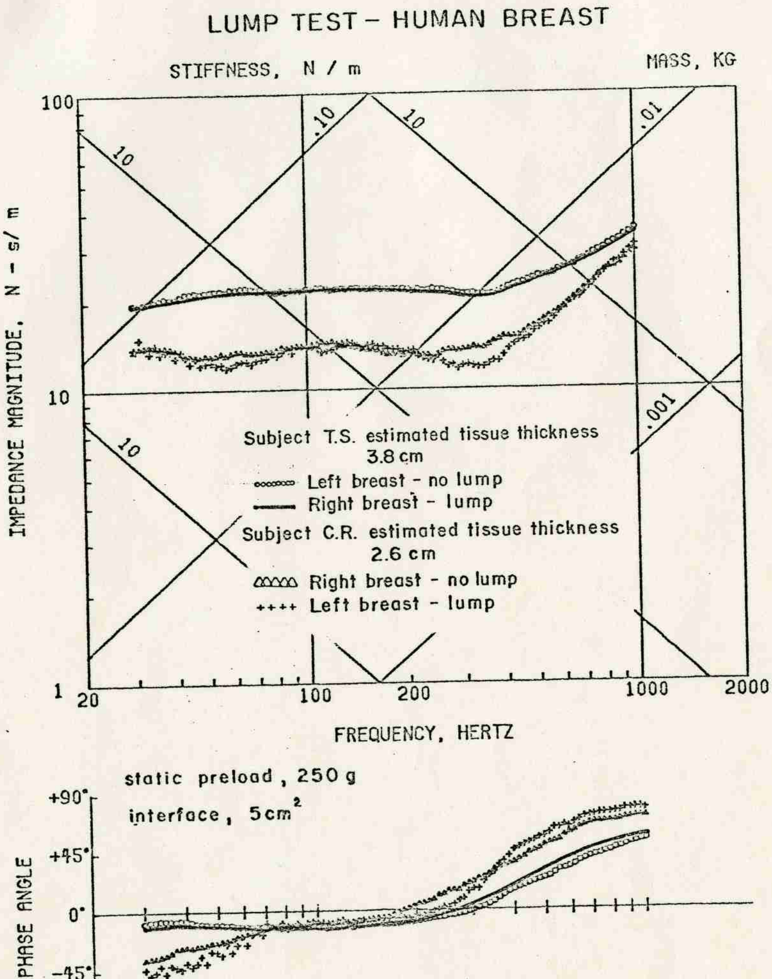

Figure 9 Impedance test on two women reporting palpable cystic lumps

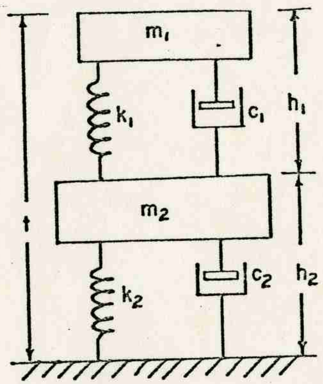

Figure 10. Physical model of soft mammary tissue used in developing predictive equation for mechanical impedance plots

impedance data. The model equation is

$$Z = (\omega m_1)_i + \frac{1}{1/(c_1 - (\frac{k_1}{\omega})i) + 1/(c_2 + (m_2\omega - \frac{k_2}{\omega})i)} \qquad \text{Eq. 5}$$

Then using a parameter fitting computer program, the model was optimized for the magnitude curves of select impedance plots. Since best fit solutions are not unique, the closeness of fit for the phase curve as well as the reasonableness of the values was used as a measure of the quality of the model. The model fit was extremely good for all animal tissue data, Figure 11.

Model parameters were found for 5 thicknesses of cow udder tissue and 5 thicknesses of human tissue, Figure 12. By associating the top three elements in the mechanical network with skin or near surface tissue and the bottom three elements with the deeper tissue, the model parameters can be related back to quasistatic values and known static properties with good agreement.

In order to evaluate the potential of driving point mechanical impedance for locating and characterizing lumps within soft tissue, the six element model was applied to the foam rubber lump test plots. These were chosen because they show the most dramatic difference between the 'with lump' and 'without lump' condition. It was found that the six element model fit the 'with lump' condition almost as well as the without lump condition, Figure 14. The largest difference in the parameter values, as would be expected, is in m_2 which increases according to the mass of the lump and k_2 which increases slightly, probably because of the additional strain in the region of the rigid lump. In terms of the real system, this would tend to indicate that the lump does not resonate significantly independently from the surrounding tissue. Careful scrutiny of the foam rubber lump test plots, Figure 13, however, reveals some shortcomings in this theory. Most importantly, in the phase curve for both 'with lump' tests, there is one distinct hump one small hump and the plot rises from 800 to 1000 Hz. This indicates the presence of at least three

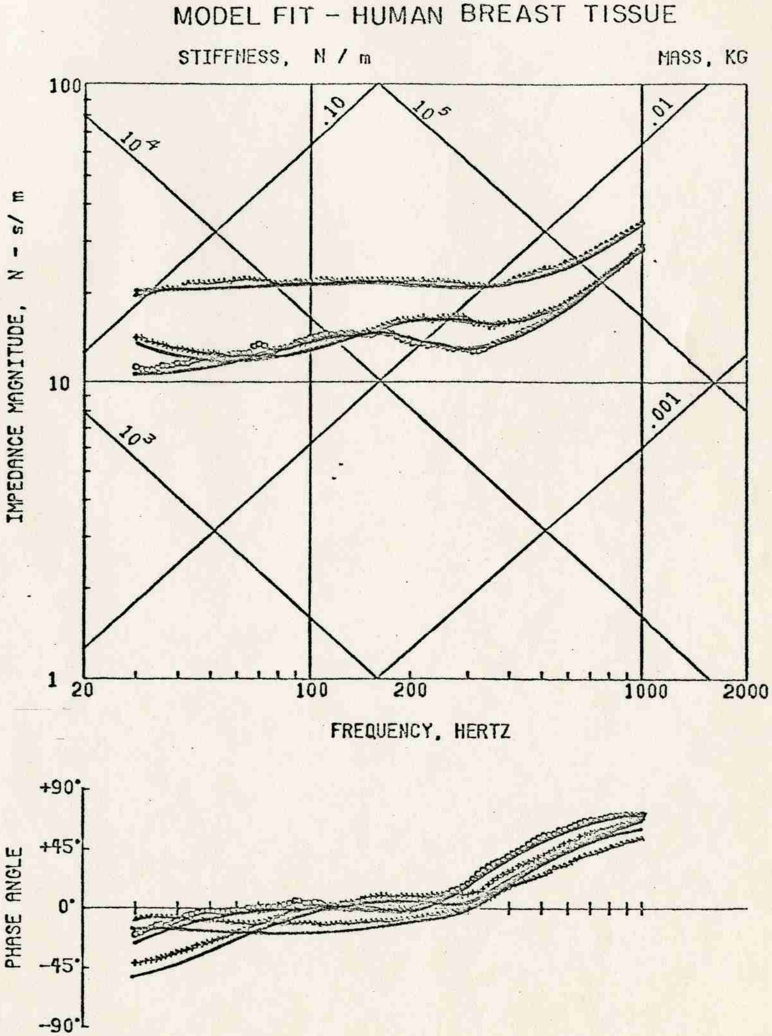

Figure 11. Observed data and theoretical models for three different thicknesses of in vivo human breast tissue

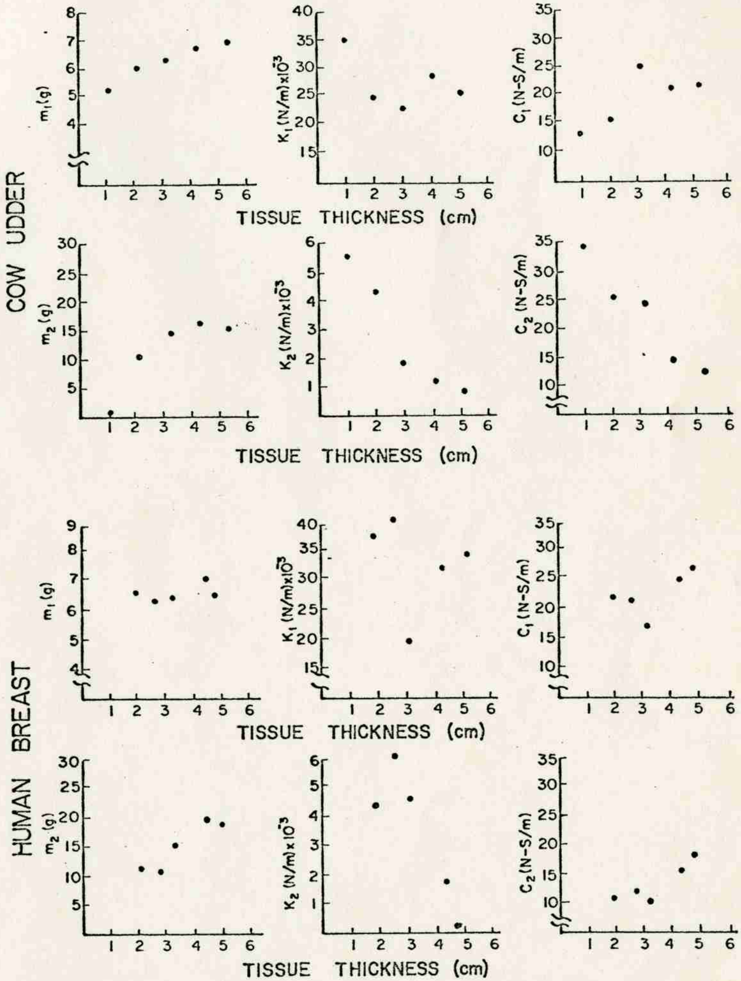

Figure 12 Cow udder and human breast model parameters shown as a function of tissue thickness

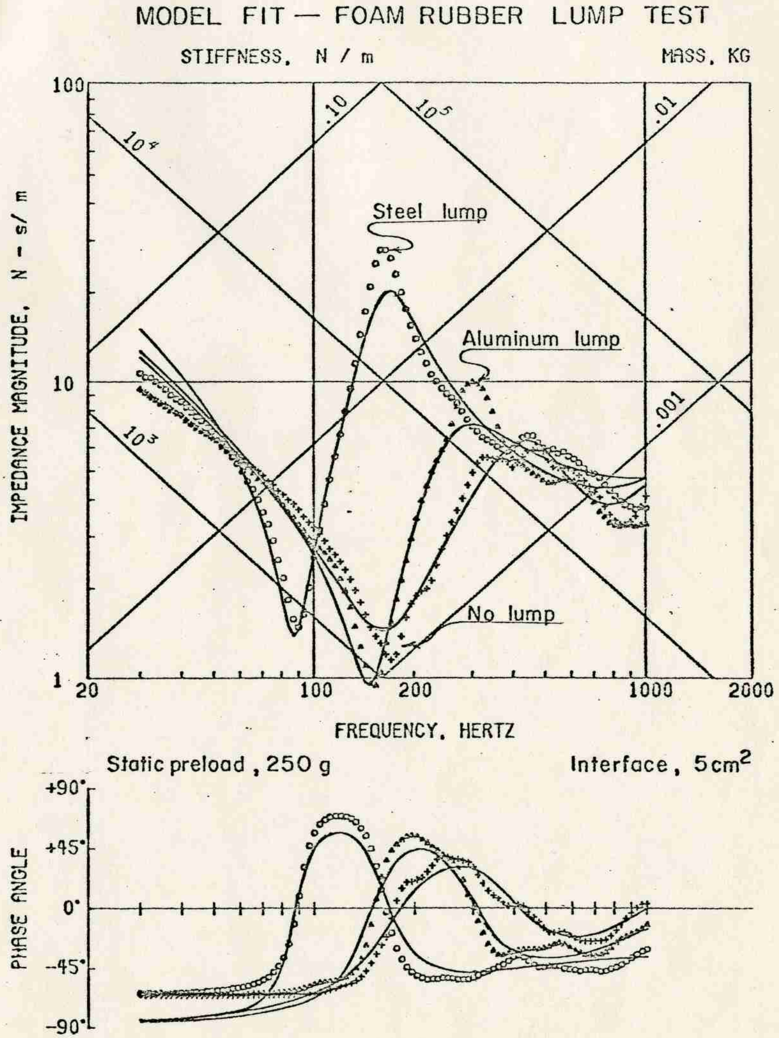

Figure 13. Observed data and theoretical model of 2-inch foam rubber lump test with 8 gram steel lump and 4 gram aluminum lump

masses. Although several nine element models were tried, none were found to yield reasonable parameters and a closer fit than the six element model. Note, however, that no presumption of nonexistence of such a model should be made on one failure to find it.

CONCLUSIONS

Carcinomas were found to be significantly stiffer than normal tissue. Some nondestructive testing technique sensitive to this change in stiffness within a continuous medium could be useful as a diagnostic tool. Mammary tissue mechanical behavior can generally be described by a highly damped six element lumped parameter viscoelastic model. The model parameters vary primarily as a function of tissue thickness. Driving point mechanical impedance techniques used to help develop the model however are inadequate to detect lumps in mammary tissue within the frequency range tested. It seems that lumps of approximately the same specific gravity as their surrounding medium tend to vibrate with the embedding tissue. Recommendations for further investigation include extending the frequency range to incorporate possible resonances above and below the range studied here, more emphasis on in vivo tissue since its vibration response is somewhat different from that of in vitro tissue, and further modeling.

LIST OF FIGURES

Figure 1. Test results for normal and pathological tissue

Figure 2. Free vibration test results: spring constant, k; natural frequency, f_n; and damping ratio, ζ; all shown as a function of loading mass.

Figure 3. Test arrangement for foam rubber lump test.

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Figure 12. Cow udder and human breast model parameters shown as a function of tissue thickness.

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A Study of Mechanical Properties of Mammary Tissue With Emphasis on Driving Point Mechanical Impedance as a Tumor Diagnostic Technique[1]

S.W. Glass and C.W. Suggs[2]
Department of Biological and Agricultural Engineering
N.C. State University
Raleigh, N.C.

ABSTRACT

Breast cancer is most frequently detected through its palpably distinguishable mechanical properties. Quasistatic compression tests, free vibration tests and driving point mechanical impedance tests were performed on foam rubber, *in vitro* cow udder and *in vivo* human mammary tissue. In the quasistatic test, serous carcinoma tumor tissue was found to have a compression modulus over three times that of normal breast tissue. In the free vibration test, the transient response of tissue to an impulse revealed that stiffness was directly related to preload on the tissue while the natural frequency and damping ratio remained constant. Driving point mechanical impedance tests on foam rubber, *in vitro*, and *in vivo* mammary tissue showed impedance to be primarily a function of tissue thickness. Lumps of steel and wood were inserted into foam rubber with a dramatic difference between 'with lump' and 'without lump' conditions. Similar *in vitro* cow udder tests showed only a small difference with the steel lump. No distinction between cystic breast lumps and normal tissue could be made. A six element lumped parameter model was fit to the observed data. It was found that the same model with slightly altered parameters fit both 'with lump' and 'without lump' systems. Based on these results, lumps of similar specific gravity to that of the surrounding soft tissue seem to vibrate with that surrounding tissue such that they are unsuitable for detection by mechanical impedance techniques. Driving point mechanical impedance cannot therefore be recommended as a feasible tumor detecting technique. There is evidence, however, to suggest further *in vivo* investigation in the region above 1000 Hz and below 30 Hz, along with more modeling and clinical tests.

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INTRODUCTION

Breast cancer is most frequently detected through its palpably distinguishable mechanical properties. In this study, certain mammary tissue mechanical properties, particularly those believed to have clinical diagnostic potential were investigated. Three types of tests were performed, quasistatic stress-strain, free vibration and driving point mechanical impedance.

Although a search of the literature to date found no references to mechanical investigation of mammary tissue, experimental and analytic techniques from investigation of other tissue types were applicable to this study. Yamada (1969) has collected a comprehensive anthology of quasistatic test results on numerous animal tissues. McElhaney's (1972) work with scalp and brain tissue, however, contains the most comprehensive quasistatic compression test results on soft tissue. In this study McElhaney also used free vibration tests and forced vibration tests similar to those used in this investigation. Suggs and Abrams (1971) emphasized driving point mechanical impedance measurement technique and the merits of lumped parameter and continuous modeling techniques in describing the nature of the biological materials. The importance of driving point mechanical impedance as a diagnostic technique has been investigated by Thompson (1973) and Entrekin (1975) in connection with the fracture and healing of the human ulnar.

QUASISTATIC UNIAXIAL COMPRESSIVE STRAIN TEST

Method

An Instron universal testing machine with a 1000 gram (9.8 newton) full scale compression load cell was used. The load cell platten was significantly larger than the sample size; the compressing piston, however, was one inch in diameter and considerabl smaller than the sample size. This is in contrast to the more traditional technique of controlling the compression area by compressing a regular cylindrical plug between two flat plates. The alternative approach was selected for four reasons. First, controlling the piston area provides much more control over the compressing area consequently reducing the variation due to different sample sizes. Second, although the actual forces measured include shear components from the forces at the piston edge, these forces are minimal for small strains compared to the uniaxial forces from beneath the piston. Although strains up to 20% were investigated, tests with foam rubber showed the compression modulus for a plug (traditional approach) to be 82% of the piston approach compression modulus value. Third, the piston contacting a region within a larger tissue sample is more representative of the way one might palpate an _in vivo_ tissue. Finally, results from this kind of test could be easily compared to the driving point mechanical impedance test results.

Tissues tested were normal and pathological cow mammary tissue and human mastectomy tissue. Samples were all prepared in the same way. A region of interest was dissected from the specimen, then a flat slab sample was sliced off with a minimum width of 5 cm and a thickness ranging from 0.5 to 3 cm. Several slicing techniques were tried but none proved very satisfactory in producing a standard size sample. This should not matter however, since the stress-strain results were normalized and therefore are a measure of intrinsic material properties in terms of unit thickness. Spot checks among similar tissue samples served to reinforce this point.

Some of the cow udder tissue samples were tested immediately after removal from the animal. Others were immersed in formalin for 15 to 20 minutes then stored dry in closed containers at room temperature overnight. This procedure simulated the history of human tissue after surgical removal and thus demonstrate the effect of the preservative.

Results and Discussion

Although a tendency for the formalin fixed udder tissue to be stiffer was noted, an f test at the 95% level showed no significant difference. Results from the fixed human tissue therefore may be assumed representative of fresh unfixed tissue. Only four carcinoma samples were tested due to the difficulty in acquiring samples. Although the variation was large, the mean slope of the stress-strain curve of the serious carcinoma tissue is over three times as great as that of normal breast stroma (Fig. 1). In order to better evaluate differences, a secant modulus estimate at 15% strain for the compression modulus was computed for each curve. Coefficients of variation and LSD values were calculated. No significant difference as a result of the formalin treatment or between fixed breast and unfixed udder stroma was found (Table 1). There was, however, a difference among breast carcinoma, bovine supramammary lymph node tissue, mastitic scar tissue; skin, and mammary stroma tissue.

A mechanical test sensitive to material stiffness may therefore be a potentially valuable diagnostic aid. Although quasistatic stress strain tests are limited to excized tissues, perhaps other techniques such as driving point mechanical impedance can be made sensitive to different stiffnesses within tissues as a non-invasive method.

FREE VIBRATION TEST

Method

By observing the decaying vibration of a material in response to a step input, the natural frequency, ω_n, damping ratio, ζ, and stiffness, k, may be estimated. Since the object of this test was only to provide a general understanding of the dynamic behavior of soft tissue, only cow udder tissue was tested.

Flat slabs of tissue 1 cm thick were prepared as in the quasistatic test and placed between horizontal 3.8 cm diameter plattens. The lower platten was connected to a piezoelectric force gage while the upper platten was loaded with increminting

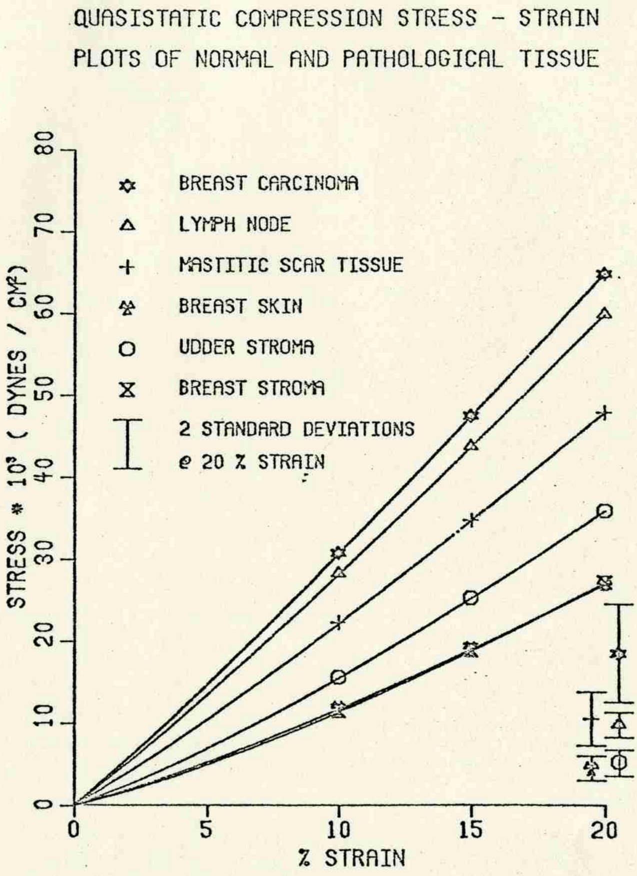

Figure 1. Test results for normal and pathological tissue

Table 1. Modulus of Compression of Various Tissue Samples.

Tissue Sample Type	Number of Observations	Number of Subjects	Modulus of Compression x 10^3 (dynes/cm^2)	Significant Difference @ .05 (LSD=14.1)	Standard Deviation	% Coefficient of Variance
Breast Carcinoma	4	4	340		60.6	17.8
				yes		
Foam Rubber	5	1	261		3.1	.011
				yes		
Lymph Node	12	3	229		25.1	10.9
				yes		
Mastitic Scar Tissue	20	5	196		18.2	9.3
				yes		
Udder Skin (Fixed)	16	4	150		10.3	6.9
				no		
Human Skin (Fixed)	4	4	141		19.6	13.9
Udder Skin (Unfixed)	20	5	139		8.6	6.2
				yes		
Udder Tissue (Fixed)	16	4	106		14.7	13.9
				no		
Udder Tissue (Unfixed)	20	5	102		14.2	14.0
				no		
Breast Stroma	9	4	89		13.8	15.5

masses from 0.1 to 0.5 kilograms. The mass was then tapped with a steel striker resulting in a decaying sinusoidal signal from the force transducer to a storage oscilloscope. For linear materials the amplitude of the step input is inconsequential since only ratios of deck magnitudes are used in the calculations. Although mammary tissue is clearly not linear as seen in the quasistatic response and the driving point mechanical impedance plots, linearity seems an acceptable assumption for the free vibration study. The damping ratio, ζ, was found by the logarithmic decrement method using

$$\ln \frac{h_1}{h_2} = 2\pi \zeta\sqrt{1 - \zeta^2} \qquad \text{Eq. 1}$$

where h_1 and h_2 represent the height of the first and second period peaks respectively. Knowing ζ, the natural frequency, can be computed from the period, t, by

$$\omega_n = \frac{1}{t\sqrt{1 - \zeta^2}} \qquad \text{Eq. 2}$$

Finally k is found from

$$k = \omega_n^2 m \qquad \text{Eq. 3}$$

Where m is mass.

Results and Discussion

Of the five udder stroma tissues sampled, the damping ratio was found to be fairly constant as the mass resting on top of the material was varied (Fig. 2a). The mean damping ratio was .0902 with a coefficient of variance of .6%. The natural frequency was also fairly constant, however, stiffness was found to increase linearly with increased mass (Figure 2b and 2c). Such behavior is in contrast to the more typical fixed stiffness and decreasing natural frequency as a function of increasing mass for the classical network representation of mechanical systems. This type of behavior might be anticipated however from the nonlinear stress-strain response. When the strain level was low (small mass) the slope, i.e., stiffness, was lower than for higher strain levels (large mass). This also indicates that the static preload will have a dramatic effect on the dynamic impedance plots.

FREE VIBRATION TEST RESULTS

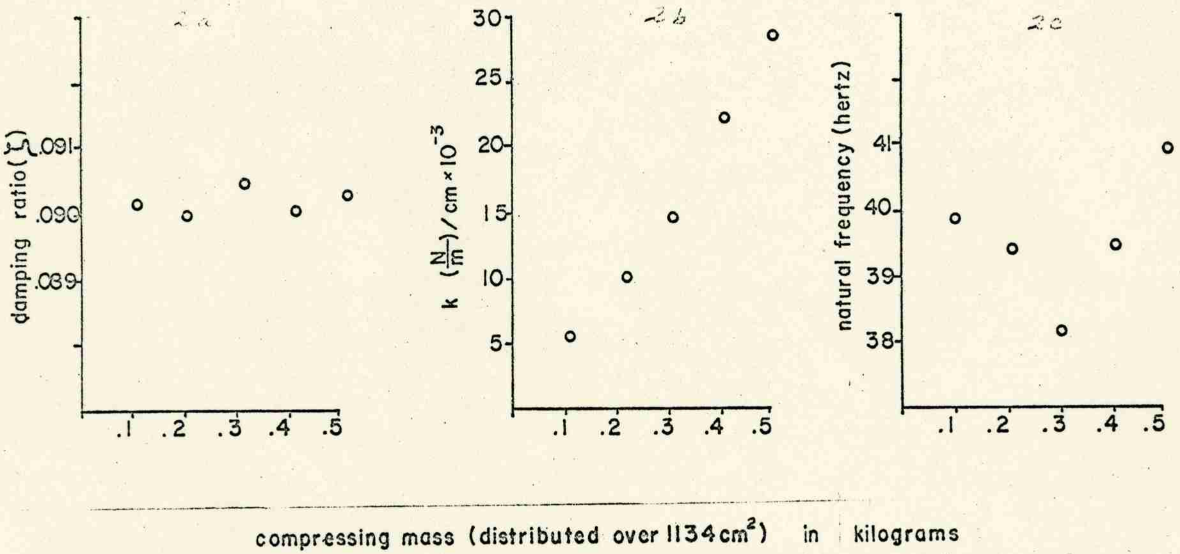

Figure 2 Free vibration test results: spring constant, k; natural frequency, f_n; and damping ratio, ζ; all shown as a function of loading mass

DRIVING POINT MECHANICAL IMPEDANCE TEST

Introduction

Driving point mechanical impedance is a complex quantity describing the ratio of the force of excitation to the resulting velocity of the system. By expressing the frequency response of impedance in polar form, it is possible to represent a continuous frequency spectrum by two, two dimensional plots, i.e. impedance magnitude versus frequency and phase angle (force with respect to velocity) versus frequency. Conveniently, this kind of representation has a family of pure mass contours with a magnitude slope of +20 db per decade and a $+90^{\circ}$ phase angle, pure spring contours with a magnitude slope of -20 db per decade and -90° phase angle and pure damping with 0 magnitude slope and 0° phase angle. This helps in modeling the response and ultimately relating the impedance plots back to the biological system.

Method

A continuous sweep, automatic computing and recording impedance measuring system was used. In response to the movement of the shaker, the A.C. force and acceleration signals from the impedance head are passed to the mass cancellation amplifier. By taking advantage of Newton's second law, the acceleration signal (which is in phase with the force signal for a pure mass) may be used to subtract the effect of the mass of the interface fixture from the total force signal. The result is a force signal of the sample object alone. After passing through a tracking filter to eliminate any nonlinear distortion, the mechanical impedance, both magnitude and phase angle, are computed and recorded on both a real time x, y, y′ plotter and on a multichannel FM tape recorder. The taped data was later digitized and stored on disks for statistical analysis and computer plotting. (Spectral Dynamics, 1974).

The shaker, resting on top of the test sample was hand steadied, figure 3. At first the static preload per unit of interface area was controlled by changing the size of the interface. Later, however, a system of counterweights was added for more precise control of the preload. For most samples, both the 20 cm^2 and the 5 cm^2 interface areas were tried. The larger interface area was less subject to local variations in mechanical properties of the foam rubber and the cow udder material however it could not adquately interface the human breast tissue due to the natural curvature of the surface. The smaller interface area showed more dramatic differences between the with lump and without lump conditions. Although static preload and interface area have a pronounced effect on the impedance magnitude, the general shape of the frequency response plot is relatively unaltered.

The acceleration level in all tests was 0.5 g (4.9 m/s^2) and the frequency range was from 30 to 1000 Hz. The upper frequency limit was guided by Mishoe (1974) and others who suggest that near surface properties dominate the response with increased frequency. The lower limit was due to limitations of the excitor system.

A small cylindrical lump (diameter 1.27 cm, height 0.635 cm), one of wood and one of steel weighing 0.8 and 8 grams respectively, was inserted into the foam rubber and the cow udder material. The lump's characteristics differed from their surrounding medium far more than would a carcinoma and therefore should be easier to diagnose. Had the animal lump tests been more conclusive, lumps which better resemble the carcinomas could have been tested.

Where it was possible and appropriate, a number of impedance plots were reduced to a single mean plot. In order to be absolutely correct, the mean value of several complex numbers must be computed from their rectangular forms at each frequency. For small differences in the phase angle however, the error introduced by computing means of each polar co-ordinate was less than 5%. Consequently this method was used.

In an attempt to reduce a group of plots to a single valued indication of variance,

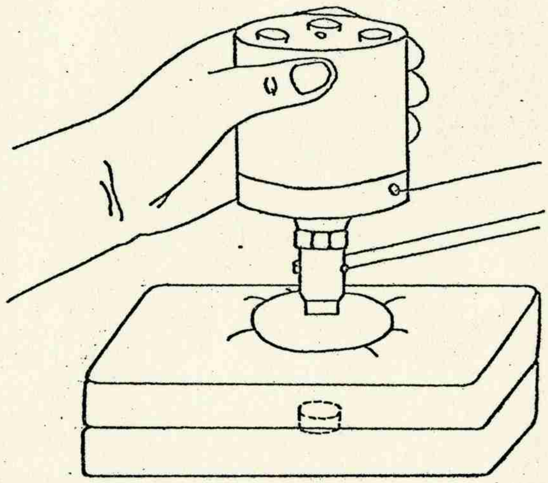

Figure 3. Test arrangement for foam rubber lump test

the mean coefficient of variance, (% $\overline{C.V.}$), was used. An average coefficient of variance was calculated from magnitude and phase at each frequency. Note that log values are used for the magnitude computations and the phase angles are offset by 90° in order to eliminate division by zero.

$$\% \overline{C.V.} = \frac{100 \times \sum_{i=1}^{n} \left(\frac{\log (\sigma_z)_i}{\log (\overline{Z})_i} + \frac{(\sigma_\phi)_i}{(\overline{\phi}_i + 90^\circ)} \right)}{n} \qquad \text{Eq. 4}$$

In Equation 4, σ is the standard deviation and $\overline{Z}$ and $\overline{\phi}$ are the mean impedance magnitude and phase angle respectively.

Results and Discussion

Foam Rubber Test

Because of its resemblance to the mechanical characteristics of mammary tissue, foam rubber was the first material tested. It was found that the sample thickness had a pronounced effect on the impedance response. Incriments of 2.54 cm from 2.54 cm to 7.62 cm were tested. With increased sample thickness, the primary resonance dropped from 600 Hz to 90 Hz, constant stiffness asymptopes were lowered, constant mass asymptopes below 500 Hz were raised, however constant mass asymptopes above 700 Hz were changed very little. This supports the claim that higher frequency response is primarily influenced by the near surface region.

In the foam rubber lump test, a dramatic difference between the impedance plots of foam rubber with and without a steel lump was noted. The wooden lump's plot was also distinguishable from that of the 'no lump' use although not nearly to the same extent, Figure 4. This implies that at least part of the lump's altered impedance resonse is related to the mass of the lump relative to the mass of the surrounding tissue. The specific gravity of the compressed foam was estimated at 0.35 compared to 0.87 for wood and over 7.0 for steel. Carcinoma tumor tissue's specific gravity however is within 10% of the surrounding stroma and therefore is not likely to be detectable if

FOAM RUBBER LUMP TEST

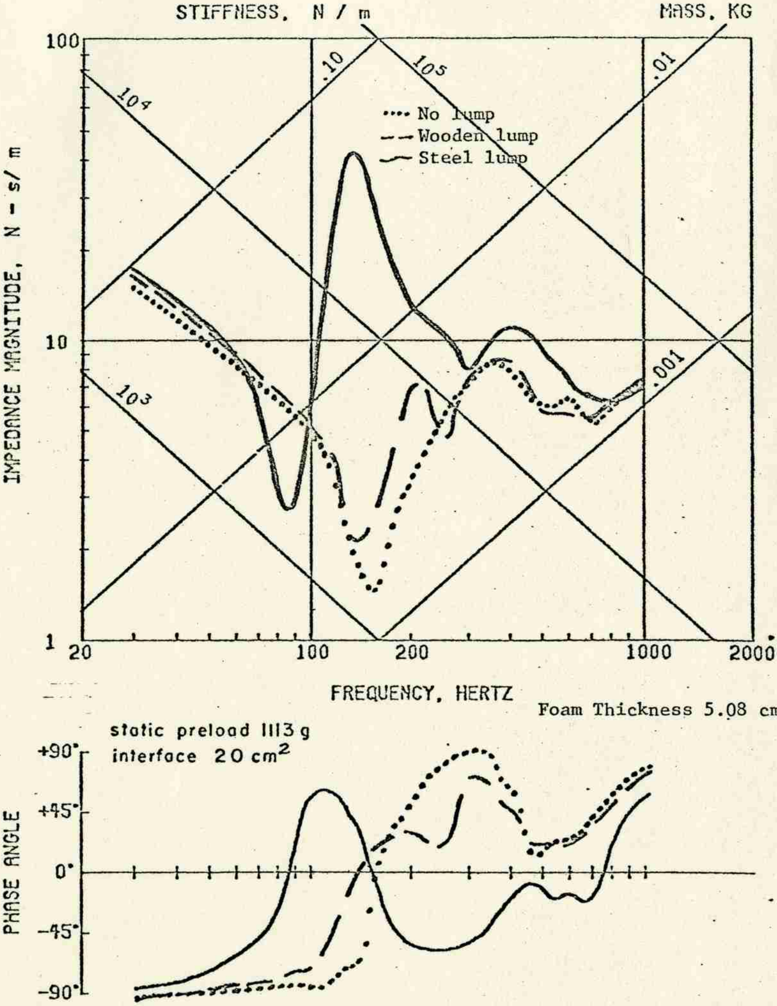

Figure 4. Foam rubber lump test for 8 g cylindrical steel lump and 1 g cylindrical wooden lump

the technique is only sensitive to specific gravity differences.

In Vitro Cow Udder Tests

In vitro cow udder tissue was also tested in much the same manner as was the foam rubber. Tissue was refrigerated immediately after necropsy then warmed to body temperature for testing. Less than 24 hours elapsed between death and the tissue test.

The first series of experiments involved measurements at several well defined anatomical locations on an intact udder. A considerable variation was found between both different anatomical locations on a single udder and between similar anatomical locations on different udders. As in the foam rubber, the most important factor in determining the mechanical impedance was the tissue thickness. In order to best show this, cow udder tissue was frozen then sawed into 1 cm incrementing thickness slabs, thawed, warmed and tested, Fig. 5.

In order to show the effect of freezing the tissue, ten samples were marked then tested both before and after the freeze procedure. An F test at the 5% level ($\alpha = 0.95$) showed no significant difference between the two classes of curves.

Lump tests were also performed on the in vitro udder tissue. Unlike the foam rubber however, three plots were made for each sample, one for the 'no lump' condition, a second for the tissue sample after an incision or 'slit' was made but before the insertion of the lump, and a third with the lump inserted into the slit. The slit was made perpendicular to the direction of vibration because it was found that this direction produced the least distorting results. Very little difference was found between the no lump condition and the light wooden lump test in the magnitude curve. The phase line, however, is distinctly different above 400 Hz for the two cm thick tissue sample, Fig. 6. The steepness of the slope at 1000 Hz indicates an additional high frequency resonance.

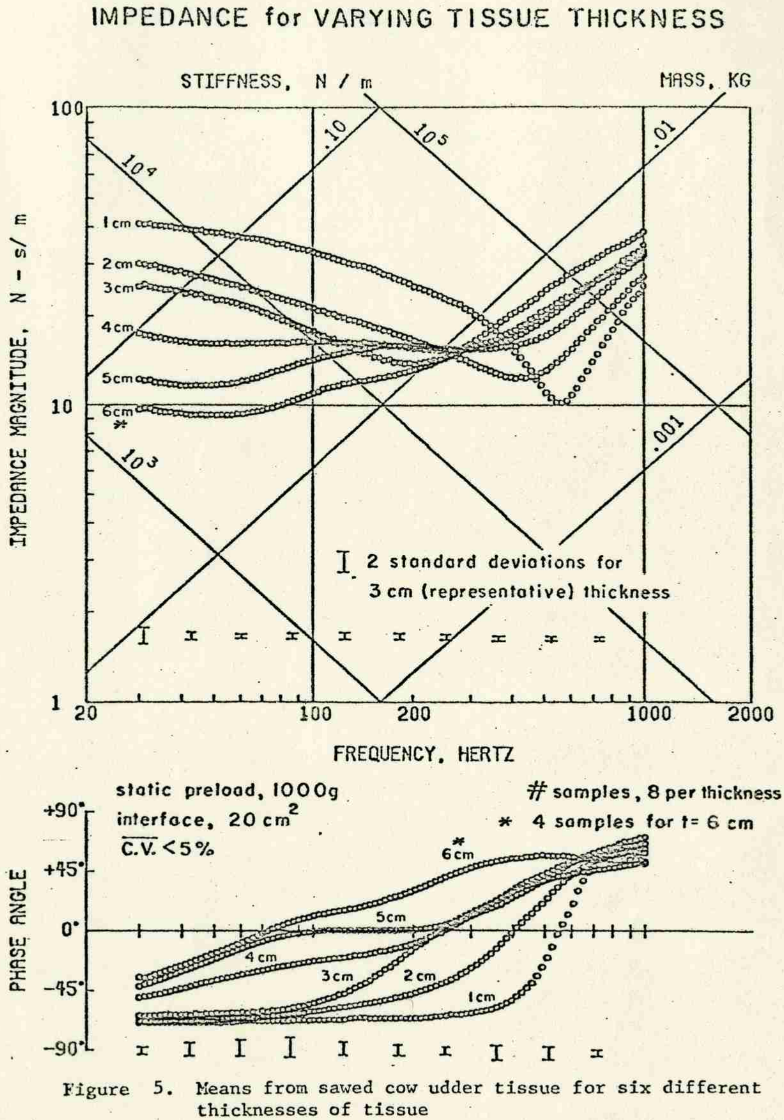

Figure 5. Means from sawed cow udder tissue for six different thicknesses of tissue

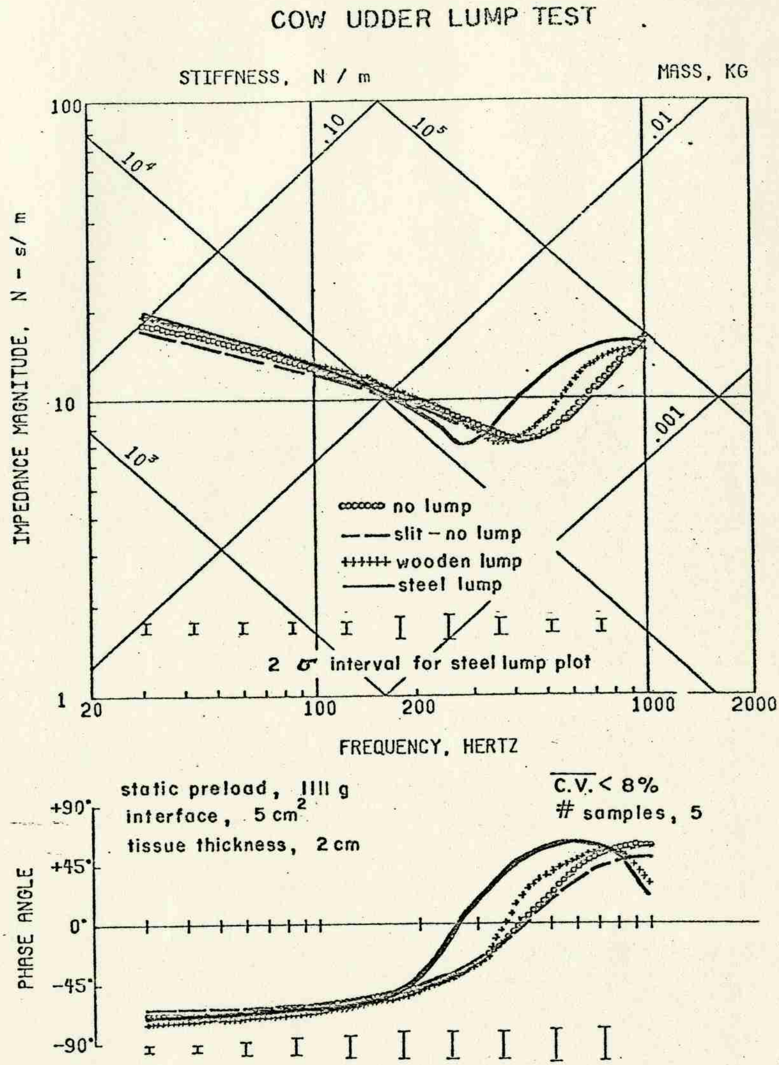

Figure 6. Means from 5 lump tests on 2 cm thick tissue for steel and wooden lumps weighing 8 and 1 g, respectively

Since differences between 'with lump' and 'without lump' impedances would be most prominant at some condition of resonance, further investigation above 1000 Hz may be worthwhile. The region below 30 Hz also may show differences since the primary resonances for the thicker udder tissues and all of the human tests seem to be below 30 Hz.

For all tissue thicknesses up to six cm, a trend of greater inflection in the steel lump plot than in the no lump plot may be noted, Fig. 7. The differences, however, are more pronounced in the thinner tissue samples. Increased degree of inflection seems the most consistent and detectable indication of a lump. Furthermore, since the degree of inflection seems related to the mass of the lump and the tissue thickness, detection of stiffness differences within the tissue is doubtful.

In Vivo Breast Tissue Test

Seven women of varying breast size, ranging in age from 21 to 31 years of age were tested. Subjects were asked to lie on their back or side such that the tangent to their ribcage at the point of excitation was parallel with the table and perpendicular to the shaking axis. Four points were tested on each breast, located above, below, medially and laterally from the nipple at a distance of three centimeters. In addition, if the subject knew of any cystic lumps, they were located and tested along with the bilaterally symetrical position.

Although in vivo tissue thickness could only be estimated, the sample thickness was found to be the most important factor in determining the nature of the impedance plot. As tissue thickness increased, however, the in vivo tissue showed a different response from that noted in the cow udder tissue. In the cow tissue, with increasing tissue thickness, the impedance magnitude for the lower frequencies (below 200 Hz) decreased. In human tissue, the plots for thicker samples tend to have less inflection and higher impedance magnitude values, Figure 8. An earlier set of experiments on goat's udders, in vivo, showed the same effect. This may represent the differences associated

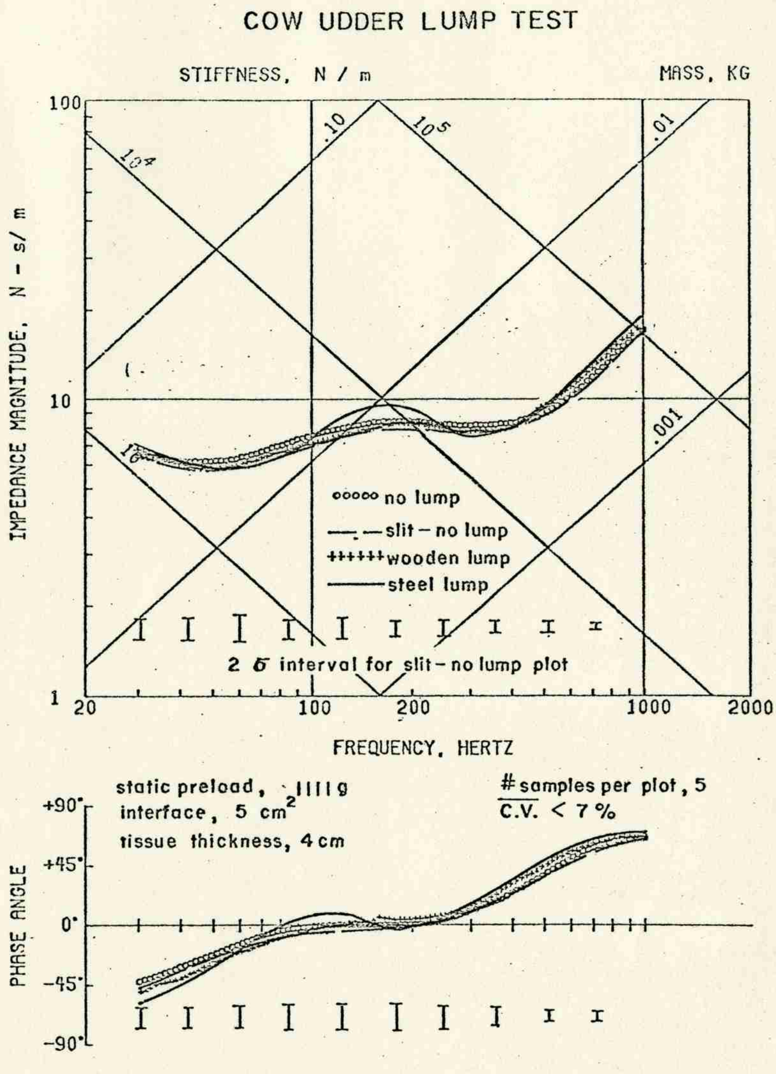

Figure 7. Means from 5 lump tests on 4 cm thick tissue for steel and wooden lumps weighing 8 and 1 g, respectively

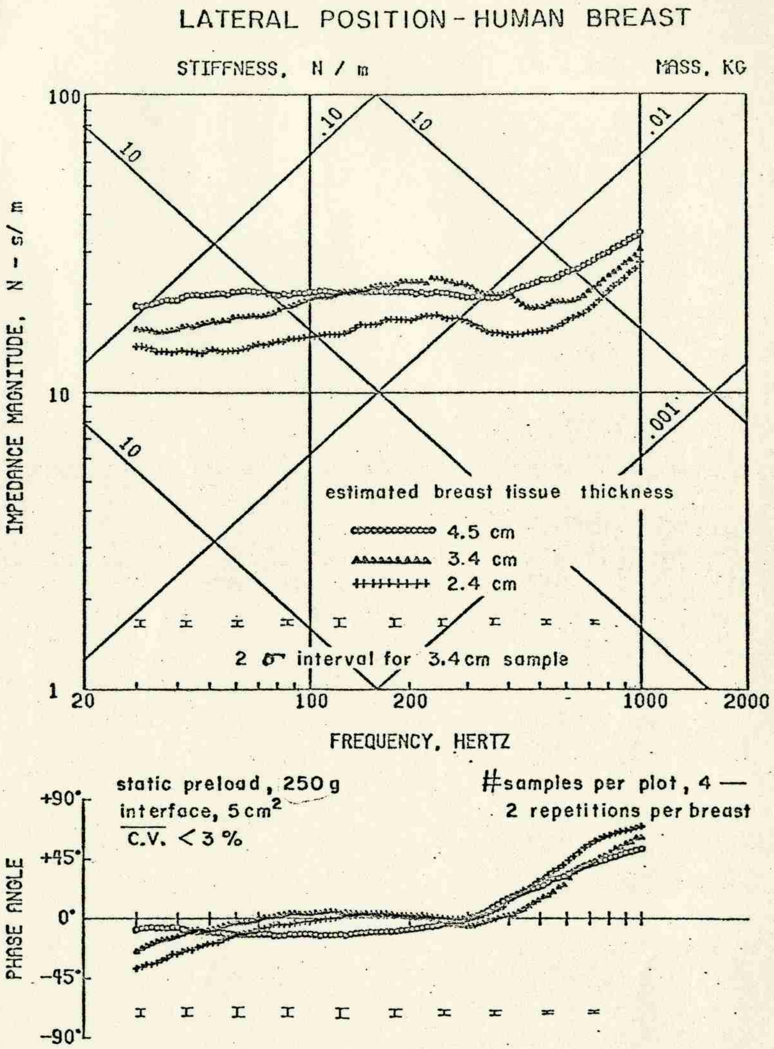

Figure 8. Lateral test position from large, medium and small breasted women

with the higher concentration of fluid in the in vivo versus the in vitro state.

Figure 9 shows two lump tests for women reporting cystic lumps. The lower magnitude curve shows the most difference between the lump condition and the no lump condition. Although the actual impedance values are very nearly the same, and there are no apparent additional resonances or antiresonances, in the lump plot, the lump curve shape has somewhat pronounced inflections and therefore indicates the lumps presence. The upper curves, however, are more typical of the lump test results among women reporting cystic lumps. No significant difference was noted at any frequency for either of the lump tests. Driving point mechanical impedance must then be considered an unpromising mammary lump detecting technique in this frequency range. Due to the one positive test, clinical trials on women with confirmed carcinomas should be considered.

A LUMPED PARAMETER MODEL FOR MAMMARY TISSUE

Unless impedance plots like those already shown can be related to the physical characteristics of the tissue and then normalized for certain sets of conditions, they are of limited use in understanding the behavior of a tissue system. By trial and error it was found that the transfer function describing the six element mechanical network of Figure 10 also generally conforms to the observed mechanical impedance data. The model equation is

$$Z = (\omega m_1)_i + \frac{1}{1/(c_1 - (\frac{k_1}{\omega})i) + 1/(c_2 + (m_2\omega - \frac{k_2}{\omega})i)} \qquad \text{Eq. 5}$$

Then using a parameter fitting computer program, the model was optimized for the magnitude curves of select impedance plots. Since best fit solutions are not unique, the closeness of fit for the phase curve as well as the reasonableness of the values was used as a measure of the quality of the model. The model fit was extremely good for all animal tissue data, Figure 11.

Model parameters were found for 5 thicknesses of cow udder tissue and 5 thicknesses of human tissue, Figure 12. By associating the top three elements in the mechanical network with skin or near surface tissue and the bottom three elements with the

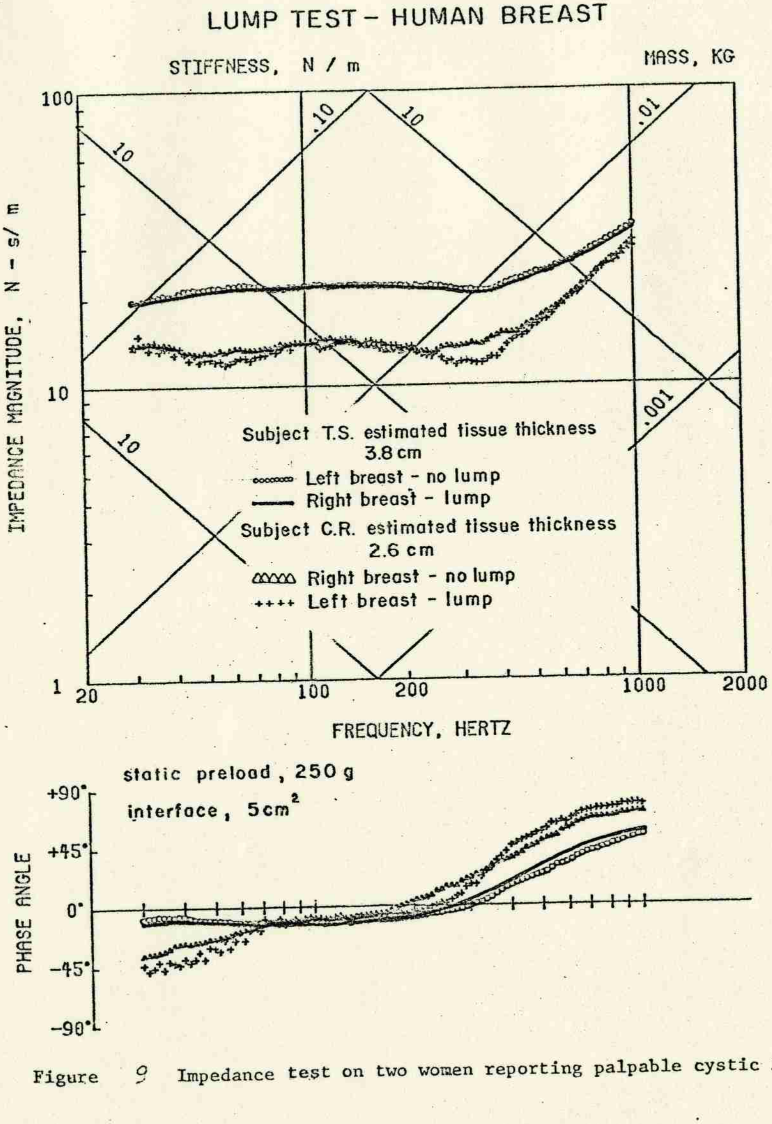

Figure 9 Impedance test on two women reporting palpable cystic lumps

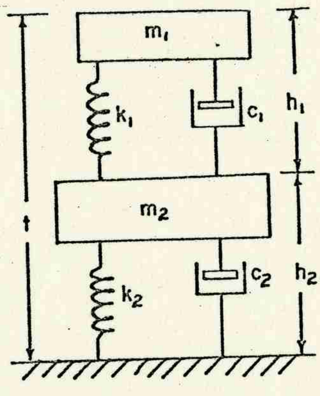

Figure 10. Physical model of soft mammary tissue used in developing predictive equation for mechanical impedance plots

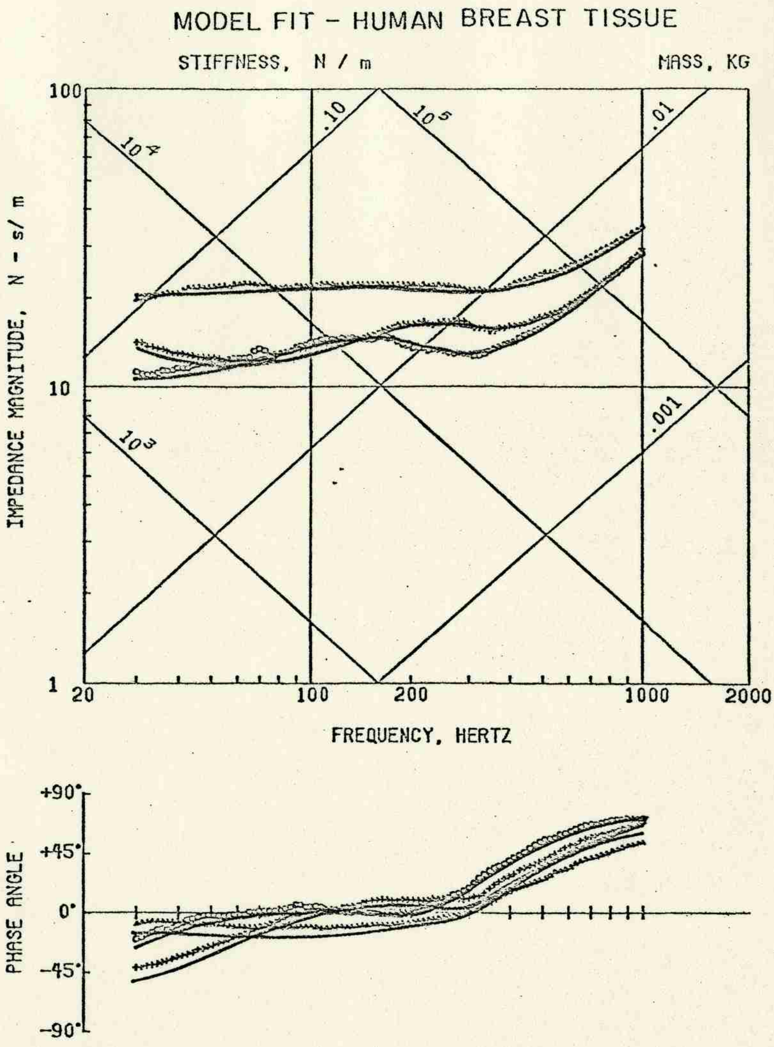

Figure 11. Observed data and theoretical models for three different thicknesses of in vivo human breast tissue

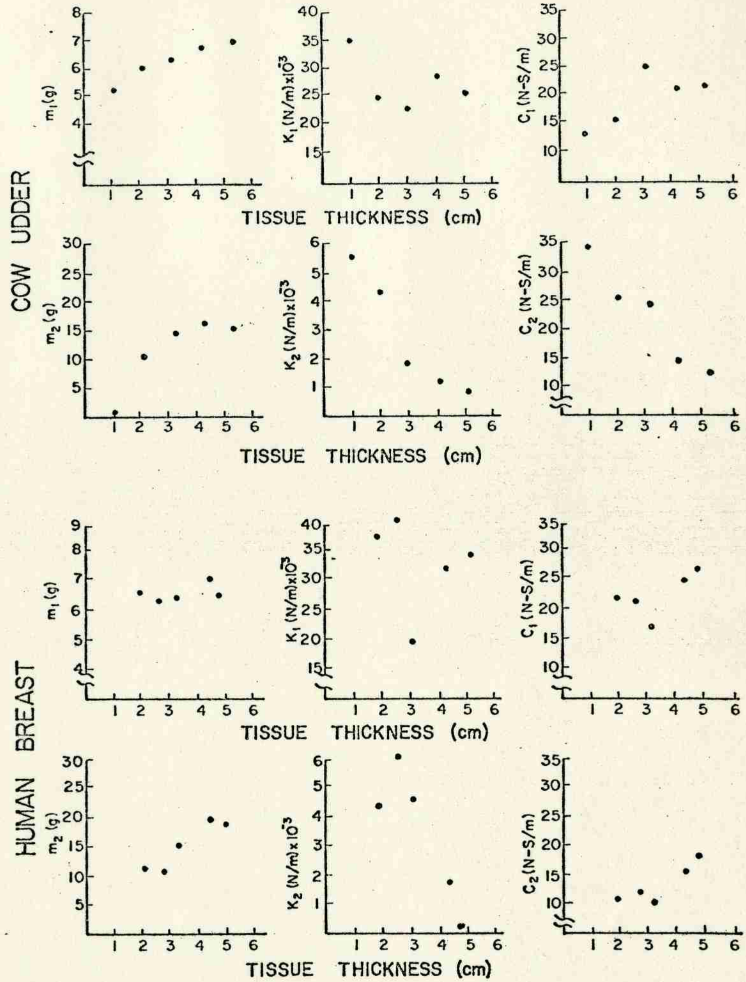

Figure 12 Cow udder and human breast model parameters shown as a function of tissue thickness

deeper tissue, the model parameters can be related back to quasistatic values and known static properties with good agreement.

In order to evaluate the potential of driving point mechanical impedance for locating and characterizing lumps within soft tissue, the six element model was applied to the foam rubber lump test plots. These were chosen because they show the most dramatic difference between the 'with lump' and 'without lump' condition. It was found that the six element model fit the 'with lump' condition almost as well as the without lump condition, Figure 14. The largest difference in the parameter values, as would be expected, is in m_2 which increases according to the mass of the lump and k_2 which increases slightly, probably because of the additional strain in the region of the rigid lump. In terms of the real system, this would tend to indicate that the lump does not resonate significantly independently from the surrounding tissue. Careful scrutiny of the foam rubber lump test plots, Figure 13, however, reveals some shortcomings in this theory. Most importantly, in the phase curve for both 'with lump' tests, there is one distinct hump one small hump and the plot rises from 800 to 1000 Hz. This indicates the presence of at least three masses. Although several nine element models were tried, none were found to yield reasonable parameters and a closer fit than the six element model. Note, however, that no presumption of nonexistence of such a model should be made on one failure to find it.

CONCLUSION

Although carcinomas are not significantly different in specific gratity from normal tissue, from the quasistatic tests and the preliminary foam rubber impedance tests. it was felt that their presence might be detected by vibratory methods. This study, however, indicated that mechanical impedance is not a feasible breast cancer tumor detecting technique because lumps with specific gravities similar to that of their surrounding medium tend to vibrate with the embedding tissue. The findings, however,

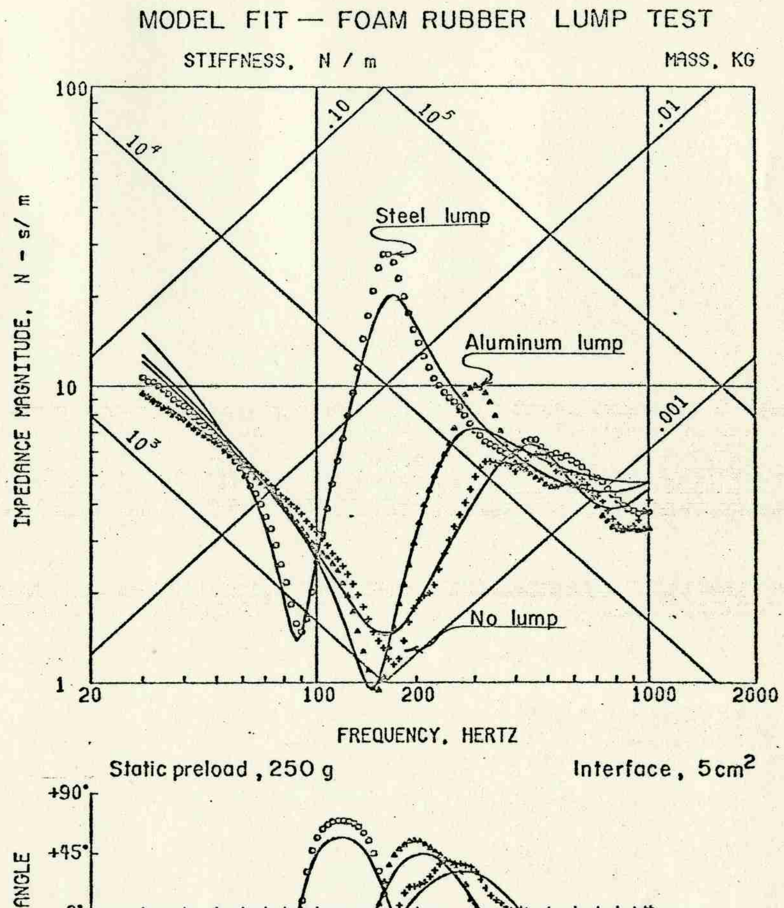

Figure 13. Observed data and theoretical model of 2-inch foam rubber lump test with 8 gram steel lump and 4 gram aluminum lump

are not conclusive and many questions should be answered before discounting the technique's use. For further investigation, the region above 1000 Hz and below 30 Hz may show significant effects. Tests on in vivo breast tissue in women with confirmed carcinomas would be more direct indication of diagnostic possibilities. Other suggestions include development of better, more complex models, surgical implantation of artificial lumps in animals for testing and the use of several transducers for locating abnormalities or lumps.

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January 18, 1978

Dr. Georgeann Eubanks
Dept. of Mechanical Engineering
Duke University
Durham, North Carolina 27766

Dear Dr. Eubanks:

In accordance with your letter of September 22, 1977 I am submitting a revision of manuscript #77-219 by S.W. Glass and myself. Mr. Glass has taken a job with the Swedish Occupational Health Institute in Stockholm and I am not sure if he sent you photographic prints of the figures or not. I will supply the necessary prints if you do not already have them.

I shall look forward to hearing from you concerning the manuscript.

Sincerely,

C.W. Suggs
Professor

CWS/bm

A Study of Mechanical Properties of Mammary Tissue With Emphasis on Driving Point Mechanical Impedance as a Tumor Diagnostic Technique[1]

before Jan 78

S.W. Glass and C.W. Suggs[2]
Department of Biological and Agricultural Engineering
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Raleigh, N.C.

ABSTRACT

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Raleigh, N.C.

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INTRODUCTION

Breast cancer is most frequently detected through its palpably distinguishable mechanical properties. In this study, certain mammary tissue mechanical properties, particularly those believed to have clinical diagnostic potential were investigated. Three types of tests were performed, quasistatic stress-strain, free vibration and driving point mechanical impedance.

Although a search of the literature to date found no references to mechanical investigation of mammary tissue, experimental and analytic techniques from investigation of other tissue types were applicable to this study. Yamada (1969) has collected a comprehensive anthology of quasistatic test results on numerous animal tissues. McElhaney's (1972) work with scalp and brain tissue, however, contains the most comprehensive quasistatic compression test results on soft tissue. In this study McElhaney also used free vibration tests and forced vibration tests similar to those used in this investigation. Suggs and Abrams (1971) emphasized driving point mechanical impedance measurement technique and the merits of lumped parameter and continuous modeling techniques in describing the nature of the biological materials. The importance of driving point mechanical impedance as a diagnostic technique has been investigated by Thompson (1973) and Entrekin (1975) in connection with the fracture and healing of the human ulnar.

QUASISTATIC UNIAXIAL COMPRESSIVE STRAIN TEST

Method

An Instron universal testing machine with a 1000 gram (9.8 newton) full scale compression load cell was used. The load cell platten was significantly larger than the sample size; the compressing piston, however, was one inch in diameter and considerab smaller than the sample size. This is in contrast to the more traditional technique of controlling the compression area by compressing a regular cylindrical plug between two flat plates. The alternative approach was selected for four reasons. First, controlling the piston area provides much more control over the compressing area consequently reducing the variation due to different sample sizes. Second, although the actual forces measured include shear components from the forces at the piston edge, these forces are minimal for small strains compared to the uniaxial forces from beneath

An Instron universal testing machine with a 1 inch diameter compressing piston (~~sig~~ considerably smaller than the sample size) was used. Samples were all prepared in the same way. A region of interest was dissected from the specimen, then a flat slab was sliced off with a minimum width of 5.0cm and a thickness ranging from 0.5 to 3.0 cm. Tissues tested were normal and pathological cow mammary tissue and human mastectomy tissue.

Tissues tested were normal and pathological cow mammary tissue and human mastectomy tissue. Samples were all prepared in the same way. A region of interest was dissected from the specimen, then a flat slab sample was sliced off with a minimum width of 5 cm and a thickness ranging from 0.5 to 3 cm. Several slicing techniques were tried but none proved very satisfactory in producing a standard size sample. This should not matter however, since the stress-strain results were normalized and therefore are a measure of intrinsic material properties in terms of unit thickness. Spot checks among similar tissue samples served to reinforce this point.

Some of the cow udder tissue samples were tested immediately after removal from the animal. Others were immersed in formalin for 15 to 20 minutes then stored dry in closed containers at room temperature overnight. This procedure simulated the history of human tissue after surgical removal and thus demonstrated the effect of the preservative.

Results and Discussion

Although a tendency for the formalin fixed udder tissue to be stiffer was noted, an f test at the 95% level showed no significant difference. Results from the fixed human tissue therefore may be assumed representative of fresh unfixed tissue. Only four carcinoma samples were tested due to the difficulty in acquiring samples. Although the variation was large, the mean slope of the stress-strain curve of the serious carcinoma tissue is over three times as great as that of normal breast stroma (Fig. 1). In order to better evaluate differences, a secant modulus estimate at 15% strain for the compression modulus was computed for each curve. Coefficients of variation and LSD values were calculated. No significant difference as a result of the formalin treatment or between fixed breast and unfixed udder stroma was found (Table 1). There was, however, a difference among breast carcinoma, bovine supramammary lymph node tissue, mastitic scar tissue; skin, and mammary stroma tissue.

A mechanical test sensitive to material stiffness may therefore be a potentially valuable diagnostic aid. Although quasistatic stress strain tests are limited to excized tissues, perhaps other techniques ~~such as driving point mechanical impedance~~ can be made sensitive to different stiffnesses within tissues as a non-invasive method.

FREE VIBRATION TEST

Method

By observing the decaying vibration of a material in response to a step input, the natural frequency, ω_n, damping ratio, ζ, and stiffness, k, may be estimated. Since the object of this test was only to provide a general understanding of the dynamic behavior of soft tissue, only cow udder tissue was tested.

Flat slabs of tissue 1 cm thick were prepared as in the quasistatic test and placed between horizontal 3.8 cm diameter plattens. The lower platten was connected to a piezoelectric force gage while the upper platten was loaded with incrementing masses from 0.1 to 0.5 kilograms. The mass was then tapped with a steel striker resulting in a decaying sinusoidal signal from the force transducer to a storage oscilloscope. For linear materials the amplitude of the step input is inconsequential since only ratios of deck magnitudes are used in the calculations. Although mammary tissue is clearly not linear as seen in the quasistatic response and the driving point mechanical impedance plots, linearity seems an acceptable assumption for the free vibration study. The damping ratio, ζ, was found by the logarithmic decrement method ~~using~~ as described by Seto ( )

$$\ln \frac{h_1}{h_2} = 2\pi \zeta\sqrt{1 - \zeta^2} \qquad \text{Eq. 1}$$

where h_1 and h_2 represent the height of the first and second period peaks respectively. Knowing ζ, the natural frequency, can be computed from the period, t, by

$$\omega_n = \frac{1}{t\sqrt{1 - \zeta^2}} \qquad \text{Eq. 2}$$

Finally k is found from

$$k = \omega_n^2 m \qquad \text{Eq. 3}$$

Where m is mass.

Results and Discussion

Of the five udder stroma tissues sampled, the damping ratio was found to be fairly constant as the mass resting on top of the material was varied (Fig. 2a). The mean damping ratio was .0902 with a coefficient of variance of .6%. The natural frequency was also fairly constant, however, stiffness was found to increase linearly with increased mass (Figure 2b and 2c). Such behavior is in contrast to the more typical fixed stiffness and decreasing natural frequency as a function of increasing mass for the classical network representation of mechanical systems. This type of behavior might be anticipated however from the nonlinear stress-strain response. When the strain level was low (small mass) the slope, i.e., stiffness, was lower than for higher strain levels (large mass). This also indicates that the static preload will have a dramatic effect on the dynamic impedance plots.

DRIVING POINT MECHANICAL IMPEDANCE TEST

Introduction

Driving point mechanical impedance is a complex quantity describing the ratio of the force of excitation to the resulting velocity of the system. By expressing the frequency response of impedance in polar form, it is possible to represent a continuous frequency spectrum by two, two dimensional plots, i.e. impedance magnitude versus frequency and phase angle (force with respect to velocity) versus frequency. Conveniently, this kind of representation has a family of pure mass contours with a magnitude slope of +20 db per decade and a $+90^{\circ}$ phase angle, pure spring contours with a magnitude slope of -20 db per decade and -90° phase angle and pure damping with 0 magnitude slope and 0° phase angle. This helps in modeling the response and ultimately relating the impedance plots back to the biological system.

Method

A continuous sweep, automatic computing and recording impedance measuring system was used. In response to the movement of the shaker, the A.C. force and acceleration signals from the impedance head are passed to the mass cancellation amplifier. By taking advantage of Newton's second law, the acceleration signal (which is in phase with the force signal for a pure mass) may be used to subtract the effect of the mass of the interface fixture from the total force signal. The result is a force signal of the sample object alone. After passing through a tracking filter to eliminate any nonlinear distortion, the mechanical impedance, both magnitude and phase angle, are computed and recorded on both a real time x, y, y′ plotter and on a multichannel FM tape recorder. The taped data was later digitized and stored on disks for statistical analysis and computer plotting. (Spectral Dynamics, 1974).

91 Because of its similar quasistatic stiffness to mammary tissue and because it was more convenient to use than animal tissue, foam rubber was used to develop most of the dynamic testing techniques. ~~The dynamic response of foam rubber was also somewhat like tissue except that~~ Except for its very low damping, foam rubber's dynamic characteristics were also similar to animal tissue. Absence of the smoothing effect of damping ~~rate~~ on the frequency profile provided a better opportunity for observation and modeling of soft material vibration behavior. These observations and models were then transferred and tested on the more subtle curves of the animal tissue.

The shaker, resting on top of the test sample was hand steadied, figure 3. At first the static preload per unit of interface area was controlled by changing the size of the interface. Later, however, a system of counterweights was added for more precise control of the preload. For most samples, both the 20 cm^2 and the 5 cm^2 interface areas were tried. The larger interface area was less subject to local variations in mechanical properties of the foam rubber and the cow udder material however it could not adquately interface the human breast tissue due to the natural curvature of the surface. The smaller interface area showed more dramatic differences between the with lump and without lump conditions. Although static preload and interface area have a pronounced effect on the impedance magnitude, the general shape of the frequency response plot is relatively unaltered.

The acceleration level in all tests was 0.5 g (4.9 m/s^2) and the frequency range was from 30 to 1000 Hz. The upper frequency limit was guided by Mishoe (1974) and others who suggest that near surface properties dominate the response with increased frequency. The lower limit was due to limitations of the excitor system.

A small cylindrical lump (diameter 1.27 cm, height 0.635 cm), one of wood and one of steel weighing 0.8 and 8 grams respectively, was inserted into the foam rubber and the cow udder material. The lump's characteristics differed from their surrounding medium far more than would a carcinoma and therefore should be easier to diagnose. Had the animal lump tests been more conclusive, lumps which better resemble the carcinomas could have been tested.

Where it was possible and appropriate, a number of impedance plots were reduced to a single mean plot. In order to be absolutely correct, the mean value of several complex numbers must be computed from their rectangular forms at each frequency. For small differences in the phase angle however, the error introduced by computing means of each polar co-ordinate was less than 5%. Consequently this method was used.

In an attempt to reduce a group of plots to a single valued indication of variance, the mean coefficient of variance, (% $\overline{C.V.}$), was used. An average coefficient of variance was calculated from magnitude and phase at each frequency. Note that log values are used for the magnitude computations and the phase angles are offset by 90^{o} in order to eliminate division by zero.

$$\% \overline{C.V.} = \frac{100 \times \sum_{i=1}^{n} \left(\frac{\log (\sigma_z)_i}{\log (\overline{Z})_i} + \frac{(\sigma_\phi)_i}{(\overline{\phi}_i + 90^o)} \right)}{n} \qquad \text{Eq. 4}$$

In Equation 4, σ is the standard deviation and $\overline{Z}$ and $\overline{\phi}$ are the mean impedance magnitude and phase angle respectively.

Results and Discussion

Foam Rubber Test

Because of its resemblance to the mechanical characteristics of mammary tissue, foam rubber was the first material tested. It was found that the sample thickness had a pronounced effect on the impedance response. Incriments of 2.54 cm from 2.54 cm to 7.62 cm were tested. With increased sample thickness, the primary resonance dropped from 600 Hz to 90 Hz, constant stiffness asymptopes were lowered, constant mass asymptopes below 500 Hz were raised, however constant mass asymptopes above 700 Hz were changed very little. This supports the claim that higher frequency response is primarily influenced by the near surface region.

In the foam rubber lump test, a dramatic difference between the impedance plots of foam rubber with and without a steel lump was noted. The wooden lump's plot was also distinguishable from that of the 'no lump' use although not nearly to the same extent, Figure 4. This implies that at least part of the lump's altered impedance resonse is related to the mass of the lump relative to the mass of the surrounding tissue. The specific gravity of the compressed foam was estimated at 0.35 compared to 0.87 for wood and over 7.0 for steel. Carcinoma tumor tissue's specific gravity however is within 10% of the surrounding stroma and therefore is not likely to be detectable if the technique is only sensitive to specific gravity differences.

In Vitro Cow Udder Tests

In vitro cow udder tissue was also tested in much the same manner as was the foam rubber. Tissue was refrigerated immediately after necropsy then warmed to body temperature for testing. Less than 24 hours elapsed between death and the tissue test.

The first series of experiments involved measurements at several well defined anatomical locations on an intact udder. A considerable variation was found between both different anatomical locations on a single udder and between similar anatomical locations on different udders. As in the foam rubber, the most important factor in determining the mechanical impedance was the tissue thickness. In order to best show this, cow udder tissue was frozen then sawed into 1 cm incrementing thickness slabs, thawed, warmed and tested, Fig. 5.

In order to show the effect of freezing the tissue, ten samples were marked then tested both before and after the freeze procedure. An F test at the 5% level ($\alpha = 0.95$) showed no significant difference between the two classes of curves.

Lump tests were also performed on the in vitro udder tissue. Unlike the foam rubber however, three plots were made for each sample, one for the 'no lump' condition, a second for the tissue sample after an incision or 'slit' was made but before the insertion of the lump, and a third with the lump inserted into the slit. The slit was made perpendicular to the direction of vibration because it was found that this direction produced the least distorting results. Very little difference was found between the no lump condition and the light wooden lump test in the magnitude curve. The phase line, however, is distinctly different above 400 Hz for the two cm thick tissue sample, Fig. 6. The steepness of the slope at 1000 Hz indicates an additional high frequency resonance.

Since differences between 'with lump' and 'without lump' impedances would be most prominant at some condition of resonance, further investigation above 1000 Hz may be worthwhile. The region below 30 Hz also may show differences since the primary resonances for the thicker udder tissues and all of the human tests seem to be below 30 Hz.

For all tissue thicknesses up to six cm, a trend of greater inflection in the steel lump plot than in the no lump plot may be noted, Fig. 7. The differences, however, are more pronounced in the thinner tissue samples. Increased degree of inflection seems the most consistent and detectable indication of a lump. Furthermore, since the degree of inflection seems related to the mass of the lump and the tissue thickness, detection of stiffness differences within the tissue is doubtful.

In Vivo Breast Tissue Test

Seven women of varying breast size, ranging in age from 21 to 31 years of age were tested. Subjects were asked to lie on their back or side such that the tangent to their ribcage at the point of excitation was parallel with the table and perpendicular to the shaking axis. Four points were tested on each breast, located above, below, medially and laterally from the nipple at a distance of three centimeters. In addition, if the subject knew of any cystic lumps, they were located and tested along with the bilaterally symetrical position.

Although in vivo tissue thickness could only be estimated, the sample thickness was found to be the most important factor in determining the nature of the impedance plot. As tissue thickness increased, however, the in vivo tissue showed a different response from that noted in the cow udder tissue. In the cow tissue, with increasing tissue thickness, the impedance magnitude for the lower frequencies (below 200 Hz) decreased. In human tissue, the plots for thicker samples tend to have less inflection and higher impedance magnitude values, Figure 8. An earlier set of experiments on goat's udders, in vivo, showed the same effect. This may represent the differences associated with the higher concentration of fluid in the in vivo versus the in vitro state.

Figure 9 shows two lump tests for women reporting cystic lumps. The lower magnitude curve shows the most difference between the lump condition and the no lump condition. Although the actual impedance values are very nearly the same, and there are no apparent additional resonances or antiresonances, in the lump plot, the lump curve shape has somewhat pronounced inflections and therefore indicates the lumps presence. The upper curves, however, are more typical of the lump test results among women reporting cystic lumps. No significant difference was noted at any frequency for either of the lump tests. Driving point mechanical impedance must then be considered an unpromising mammary lump detecting technique in this frequency range. Due to the one positive test, clinical trials on women with confirmed carcinomas should be considered.

A LUMPED PARAMETER MODEL FOR MAMMARY TISSUE

Unless impedance plots like those already shown can be related to the physical characteristics of the tissue and then normalized for certain sets of conditions, they are of limited use in understanding the behavior of a tissue system. By trial and error it was found that the transfer function describing the six element mechanical network of Figure 10 also generally conforms to the observed mechanical impedance data. The model equation is

$$Z = (\omega m_1)_i + \frac{1}{1/(c_1 - (\frac{k_1}{\omega})i) + 1/(c_2 + (m_2\omega - \frac{k_2}{\omega})i)} \qquad \text{Eq. 5}$$

Then using a parameter fitting computer program, the model was optimized for the magnitude curves of select impedance plots. Since best fit solutions are not unique, the closeness of fit for the phase curve as well as the reasonableness of the values was used as a measure of the quality of the model. The model fit was extremely good for all animal tissue data, Figure 11.

Model parameters were found for 5 thicknesses of cow udder tissue and 5 thicknesses of human tissue, Figure 12. By associating the top three elements in the mechanical network with skin or near surface tissue and the bottom three elements with the deeper tissue, the model parameters can be related back to quasistatic values and known static properties with good agreement.

In order to evaluate the potential of driving point mechanical impedance for locating and characterizing lumps within soft tissue, the six element model was applied to the foam rubber lump test plots. These were chosen because they show the most dramatic difference between the 'with lump' and 'without lump' condition. It was found that the six element model fit the 'with lump' condition almost as well as the without lump condition, Figure 14. The largest difference in the parameter values, as would be expected, is in m_2 which increases according to the mass of the lump and k_2 which increases slightly, probably because of the additional strain in the region of the rigid lump. In terms of the real system, this would tend to indicate that the lump does not resonate significantly independently from the surrounding tissue. Careful scrutiny of the foam rubber lump test plots, Figure 13, however, reveals some shortcomings in this theory. Most importantly, in the phase curve for both 'with lump' tests, there is one distinct hump one small hump and the plot rises from 800 to 1000 Hz. This indicates the presence of at least three masses. Although several nine element models were tried, none were found to yield reasonable parameters and a closer fit than the six element model. Note, however, that no presumption of nonexistence of such a model should be made on one failure to find it.

CONCLUSION

Although carcinomas are not significantly different in specific gratity from normal tissue, from the quasistatic tests and the preliminary foam rubber impedance tests. it was felt that their presence might be detected by vibratory methods. This study, however, indicated that mechanical impedance is not a feasible breast cancer tumor detecting technique because lumps with specific gravities similar to that of their surrounding medium tend to vibrate with the embedding tissue. The findings, however, are not conclusive and many questions should be answered before discounting the technique's use. For further investigation, the region above 1000 Hz and below 30 Hz may show significant effects. Tests on in vivo breast tissue in women with confirmed carcinomas would be more direct indication of diagnostic possibilities. Other suggestions include development of better, more complex models, surgical implantation of artificial lumps in animals for testing and the use of several transducers for locating abnormalities or lumps.

Conclusions

Carcinomas were found to be significantly stiffer than normal tissue. Some nondestructive testing technique sensitive to this change in stiffness within a continuous medium could be useful as a diagnostic ~~aid~~ tool. Mammary tissues mechanical behavior can generally be described by a highly damped six element lumped parameter viscoelastic model. The model parameters vary primarily as a function of tissue thickness. ~~The~~ Driving point mechanical impedance techniques used to help develop the model however are inadiquate to detect lumps in mammary tissue within the frequency range tested. It seems that lumps of aproximately the same specific gravity as their surrounding medium tend to vibrate with the embedding tissue. Recomendations for further investigation include extending the frequency range to incorporate possible resonances above and below the range studied here, more emphasis ~~research~~ on invivo tissue since its vibration response is somewhat different from that of invitro tissue, and further modeling.

Journal of BIOMECHANICS

22 September 1977
MS 77-219

S.W. Glass
Dept. Biological and Agricultural Engr.
N.C. State University
Raleigh, NC.

Dear Dr. Glass:

I am enclosing with this letter the referee comment forms which we have received regarding your manuscript. If you will make the requested revisions in the copy, I will resubmit the paper for reviewing. I hope the comments are agreeable to you.

Please contact me if you have any questions.

Sincerely,

Georgann Eubanks

Georgann Eubanks
Editorial Assistant

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Journal of BIOMECHANICS

REFEREE REPORT

MS 77-219

TITLE:

A STUDY ON THE MECHANICAL PROPERTIES OF MAMMARY TISSUE WITH EMPHASIS ON DRIVING POINT MECHANICAL IMPEDANCE AS A TUMOR DIAGNOSTIC TECHNIQUE

AUTHOR:

S.W. SUGGS AND C.W. GLASS

Referee Decision		
	ACCEPT	☐
	RETURN FOR REVISION	☐
	REJECT - UNSUITABLE	XX

Referee Comments:

Authors present no evidence or logic that suggest that the tests performed would be expected to provide evidence of breast cancer; neither do they establish that existing methods of detection are inadequate. The growing use (and effectiveness) of radiographic and ultrasonic methods are not mentioned.

He doesn't understand M. Imp.

Foam rubber is used "because of its resemblance to the mechanical characteristics of mammary tissue," but the "resemblance" is neither specific nor documented by reference; in fact, their data (Fig. 4 vs Fig 9) indicate that there is little resemblance between human breast tissue and foam rubber.

If the specific gravity of tumor tissue is within 10% of that of surrounding tissue, why was this not simulated in the foam rubber? The logic in using lumps (in the foam rubber) with specific gravities from 2 to 20 times greater than the surrounding material is not obvious.

Generally, the methods and techniques of testing, as well as the analysis, appear valid and well done; however, the paper, in its present form, is weak. If the work were presented as a basic study of tissue properties, and not tied so strongly to breast cancer as a justification, it would form the basis of a much better paper.

Date:____________________ Signed:____________________

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Journal of BIOMECHANICS

REFEREE REPORT MS 77-219

TITLE: ~~A STUDY OF THE~~ MECHANICAL PROPERTIES OF MAMMARY TISSUE WITH EMPHASIS ON DRIVING POINT MECHANICAL IMPEDANCE ~~AS A TUMOR DIAGNOSTIC TECHNIQUE~~

AUTHOR: S.W. GLASS & C.W. SUGGS

Referee Decision

ACCEPT	☐
RETURN FOR REVISION	☒
REJECT - UNSUITABLE	☐

Referee Comments:

The paper entitled "A Study of Mechanical Properties of Mammary Tissue with Emphasis on Driving Point Mechanical Impedance as a Tumor Diagnostic Technique" by Glass and Suggs reports an interesting attempt in applying mechanical impedance as a tumor diagnostic technique. Unfortunately, the results are mostly negative and should therefore probably not be published as a full length paper but as a Technical Note.

Date:________________ Signed:________________

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Seto

In Response to Referee Comments

The suggestion to shift the emphasis from a diagnostic technique feasability study to a more general study of tissue properties is very good and is, in fact, a much better representation of the experiments intention. It is only because carcinomas are detected by their mechanical properties in palpation tests that a study of this nature has some possible practical interest. In accordance with the referees' comment the text was reviewed and rewritten.

Although some reference to existing diagnostic techniques might be desirable in a diagnostic feasability study, it was felt that such comments are inappropriet in a general tissue properties investigation report.

With regard to the reasoning behind using foam rubber, a short paragraph was inserted in the Driving Point Mechanical Impedance Method section.

A statement regarding the selection of lumps may be found in paragraph following the inserted one as mentioned above.

Title and Abstract.

<u>Consider</u> changing title to:

A STUDY OF MECHANICAL PROPERTIES OF MAMMARY TISSUE WITH EMPHASIS ON DRIVING POINT MECHANICAL IMPEDANCE AND THE EFFECT OF A LUMP WITHIN THE TISSUE

Delete First sentence: 'Breast cancer ... mechanical properties.

Abstract should begin with ' Quasistatic compression ...

Delete Next to last sentence in abstract:
' Driving point mechanical impedance cannot ... technique'

Although breast cancer ... mechanical properties, a literature search to date found no references to quantitative mechanical investigation of mammary tissue. In this study, certain ... mechanical impedance.

Delete: Although a search of the literature ... to this study

Yamada (1969) has collected ... test results on soft tissue. In his study McElhaney ...

Delete first and second paragraph under Method, Quasistatic Uniaxial C.S.T.

[Page 3]

Bottom line demonstrate → demonstrated

[Page 4]

Delete in Results & Discussion, par 2.: 'such as driving point mechanical impedance'

Sentence should now read; 'Although quasistatic stress strain tests are limited to excized tissues, perhaps other techniques can be made sensitive to different stiffnesses within tissues as a non-invasive method.'

Page 6

✓ The damping ratio, ~~ζ~~ ζ, was found by the logarithmic decrement method as described by Seto (   ).

{Note: perhaps there is a better reference ~ I dont know. The procedure is certainly in the Schaum outline by Seto}

~~Lost three equations~~

Delete the rest of that paragraph.

Begin again with 'Results and Discussion'

Page 8

✓ end of first paragraph change "is relatively altered" to "is relatively unaltered"

Insert the following paragraph between paragraph #2 & #3 of this page

... limitations of the excitor system.

A small cylindrical ...

Page 9

Under Results & Discussion: Delete First sentence "Because of its Resemblance ... material tested.

[Page 13]

Delete Conclusion - Replace with new conclusion as below

Conclusion

References

Insert additional reference as mentioned on page 6 revision

By William Glass

Driving Point Mechanical Impedance
Properties of Mammary Tissue with Emphasis
on Tumor Diagnostic Potential

INTRODUCTION

Breast cancer, bovine mastitis, and other pathologies of the mammary gland are most frequently detected through their palpably distinguishable mechanical properties. In an effort to better define certain mechanical properties of mammary tissue, the frequency response of driving point mechanical impedance for foam rubber, in vitro cow udder material, and in vivo human breast tissue was investigated.

Driving point mechanical impedance as a technique for investigating biological materials in general is discussed by Suggs and Abrams (1971). Two areas particularly emphasized include the measurement technique and the merrits of lumped parameter and continuous modeling techniques in describing the nature of the material. The possibilities of using driving point mechanical impedance as a diagnostic technique has been investigated by Thompson (1973) and Entrekin (1975) in connection with the fracture and healing of the human ulnar. McElhaneys (1972) work with scalp and brain tissue, however, contains the most extensive report of impedance responses of soft tissue to date.

The frequency response of driving point mechanical impedance (the complex quantity describing the ratio of force to velocity) is a very sensitive measure of certain mechanical characteristics. By expressing the impedance response in polar form, it is possible to represent a continuous frequency spectrum by two, two dimensional plots, i.e. impedance magnitude versus frequency and phase angle (force with respect to velocity) versus frequency. Conveniently, this kind of representation has a family of pure mass contours with a magnitude slope of +20 db per decade and $+90^{\circ}$ phase angle, pure spring contours with a magnitude slope of

-20 db per decade and -90° phase angle, and pure damping with 0 magnitude slope and 0° phase angle. This helps in modeling the response and ultimately relating the impedance plots back to the biological system.

Instrumentation and Data Reduction

A continuous sweep, automatic computing and recording impedance measuring system was used, Figure 1. In response to the movement of the shaker, the A.C. force and acceleration signals from the impedance head are passed to the mass cancellation amplifier. By taking advantage of Newton's second law, the acceleration signal (which is in phase with the force signal for a pure mass) may be used to subtract the effect of the mass of the interface fixture from the total force signal. The result is a force signal of the sample object alone. After passing through a tracking filter to eliminate any nonlinear distortion, the mechanical impedance, both magnitude and phase angle, are electronically computed and recorded on both a real time x, y, y' plotter and on a multichannel FM tape recorder. The tape was later digitized and stored on disks for statistical analysis and computer plotting.

Where it was possible and appropriate, a number of impedance plots were reduced to a single mean plot.

(No paragraph) A single valued indication of variance, the mean coefficient of variance ($\% \overline{C.V.}$) was then found.

$$\% \overline{C.V.} = \frac{100 \times \sum_{i=1}^{n} \left(\frac{\log (\sigma_z)_i}{\log (\bar{Z})_i} + \frac{(\sigma_\phi)_i}{(\bar{\phi}_i + 90^{\circ})} \right)}{n} \qquad \text{Eq. 1}$$

In Equation 1, σ is the standard deviation and $\bar{Z}$ and $\bar{\phi}$ are the mean impedance magnitude and phase angle respectively. Note that log values are used for the magnitude computations and the phase angles are offset by 90° in order to eliminate division by zero.

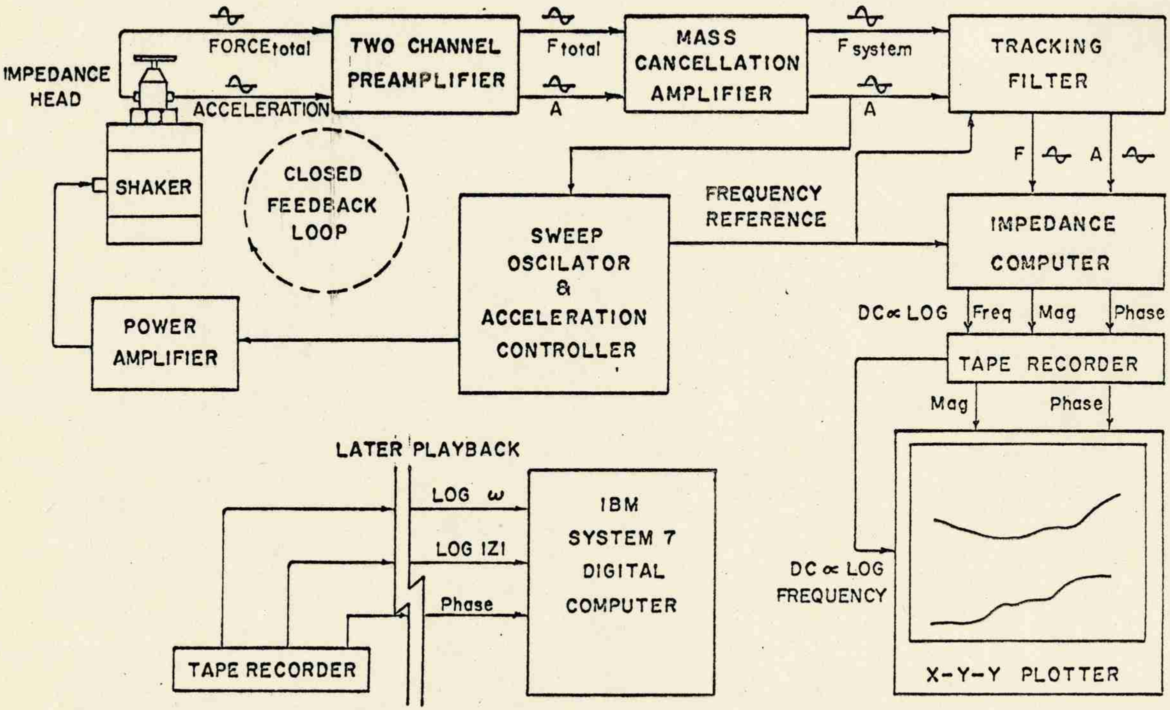

Figure 3 Automated driving point mechanical impedance measurement system

Foam Rubber Tests

Because of it's convenience and it's resemblence to the mechanical characteristics of mammary tissue, foam rubber was the first sample tested. The shaker, resting on top of the sample slab, was hand steadied, Figure 2. The static preload per unit of interface area was controlled by changing the size of the interface.

Since most mammary pathologies are characterized by lumps, small artificial lumps of steel, aluminum and wood were inserted into the foam rubber and the in vitro cow udder material and compared with the no lump condition. The foam rubber lump test shows the effect of inserting 1/2 inch diameter by 1/4 inch length cylinders (lumps) of steel and wood weighing 8 and 1 gram respectively, into a 2 inch thickness of foam rubber, Figure 3. In the case of the steel lump, there is a dramatic antiresonance or magnitude peak at 130 Hz. Also, the primary resonance at 85 Hz is shifted down from the no lump condition. In the wooden lump case, there is also an antiresonance. It is not as dramatic, however, as that of the heavier steel lump. The primary resonance is also shifted down slightly from the no lump condition. In general the difference between the impedance plots of foam rubber with and without a steel lump is quite evident. The difference between foam rubber with and without a wooden lump is not very large. Tests were done for several different sample thicknesses. Although the relative differences between the no lump and the lumped plot are similar, the shape and position of the curve changes with sample thickness.

In Vitro Cow Udder Tests

In vitro cow udder tissue was also tested, in much the same manner as was the foam rubber. Tissue was refrigerated immediately after nacropsy then warmed to body temperature for testing. Less than 24 hours elapsed between death and the tissue test.

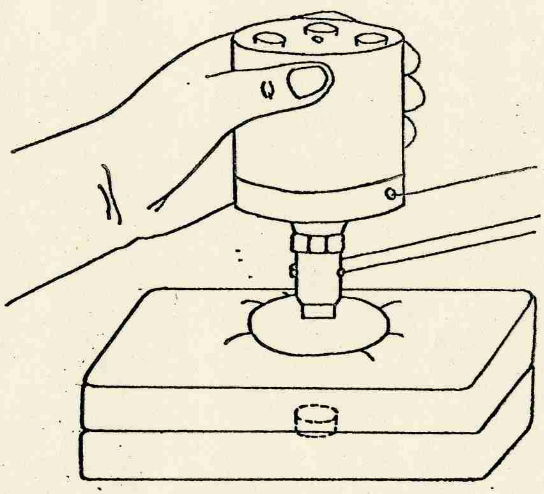

Figure 2 Test arrangement for foam rubber lump test

The first series of experiments involved measurements at several well defined anatomical locations on an intact udder. A considerable variation was found between both different anatomical locations on a single udder and between similar anatomical locations on different udders. As in the foam rubber, the most important factor in determining the mechanical impedance was the tissue thickness. In order to best show this, cow udder tissue was frozen then sawed into 1 cm incrementing thickness slabs, and tested, Figure 4. It was also noted that freezing the tissue had a negligible effect on the mechanical impedance response.

Lump tests were also performed on the in vitro udder tissue. Unlike the foam rubber, however, three plots were made for each sample, one for the 'no lump' condition, a second for the tissue sample after an incision or 'slit' was made but before the insertion of the lump, and a third with the lump inserted into the slit. Very little difference was found between the no lump condition and the light wooden lump test in the magnitude curve. The phase line, however, is distinctly different above 400 Hz for the two cm thick tissue sample, Figure 5. The steepness of the slope at 1000 Hz indicates an additional high frequency resonance. Further investigation above 1000 Hz would be needed to determine a significant difference between the 'with lump' and 'no lump' plots. For all tissue thicknesses up to six cm, a difference between the 'no lump' and the steel lump plot may be noted. The differences, however, are more pronounced in the thinner tissue samples.

In Vivo Breast Tissue Test

Seven women of varying breast size, ranging in age from 21 to 31 years of age were tested. Subjects were asked to lie on their back or side such that the tangent to their ribcage at the point of excitation was parallel with the table and perpendicular to the shaking axis. Four points were tested on each breast, 7

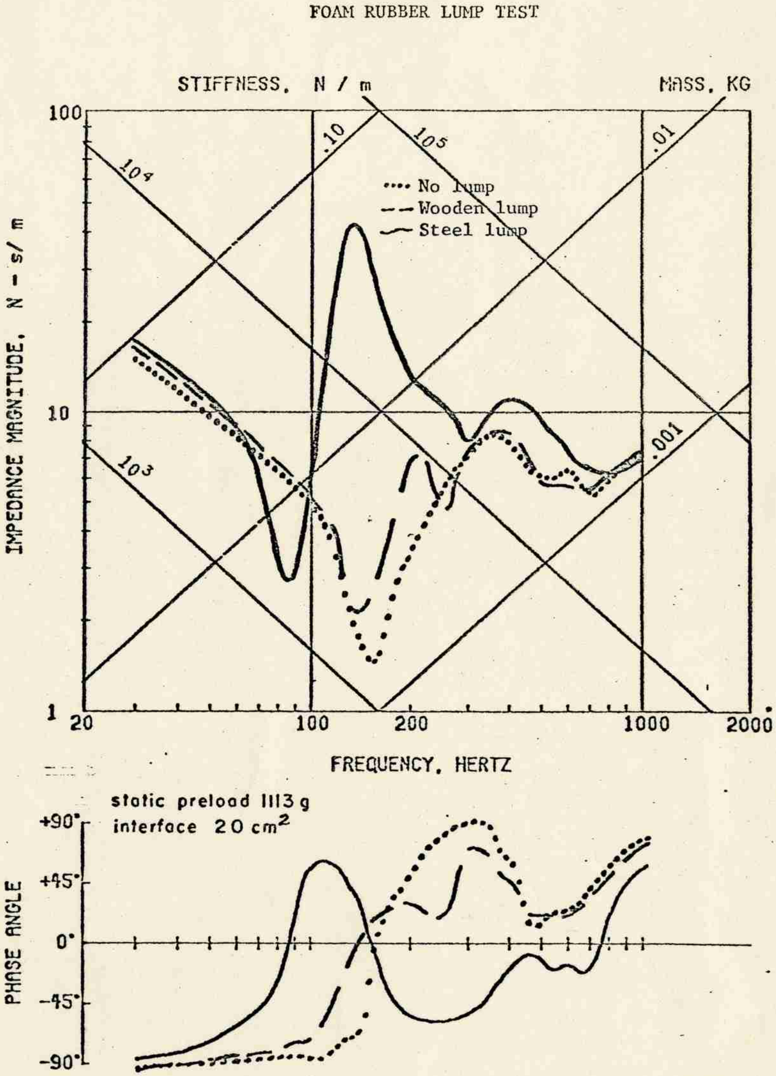

Figure 5 Foam rubber lump test for 8 g cylindrical steel lump and 1 g cylindrical wooden lump

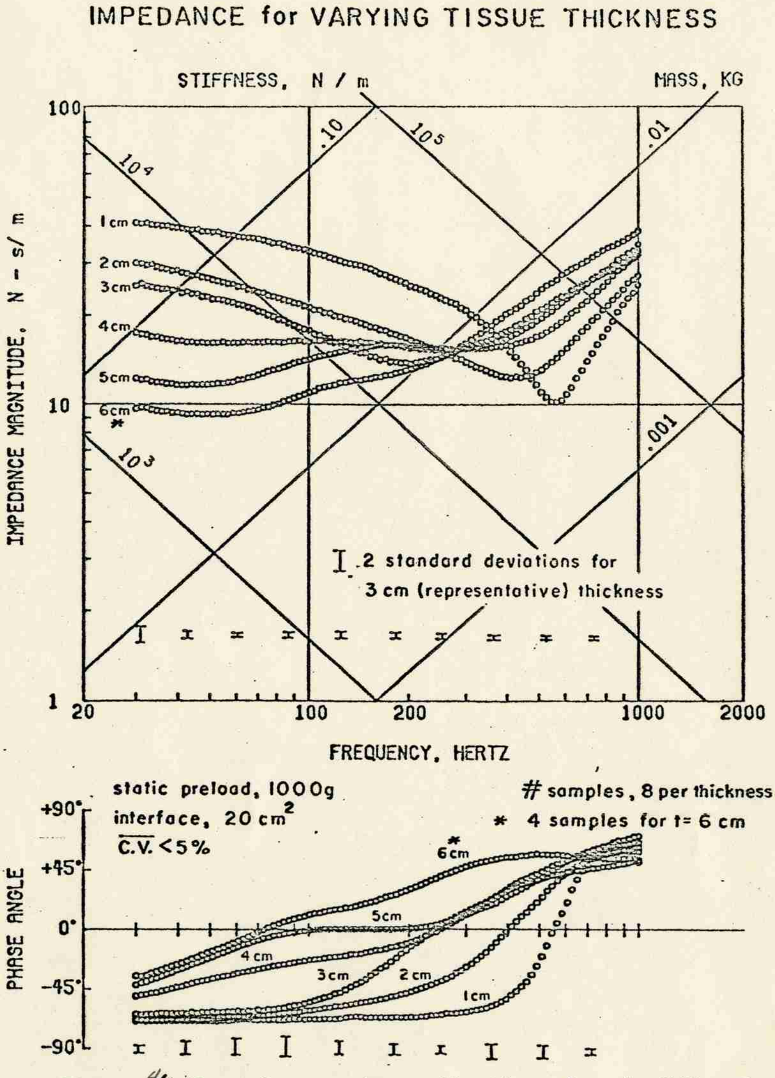

Figure 4b Means from sawed cow udder tissue for six different thicknesses of tissue

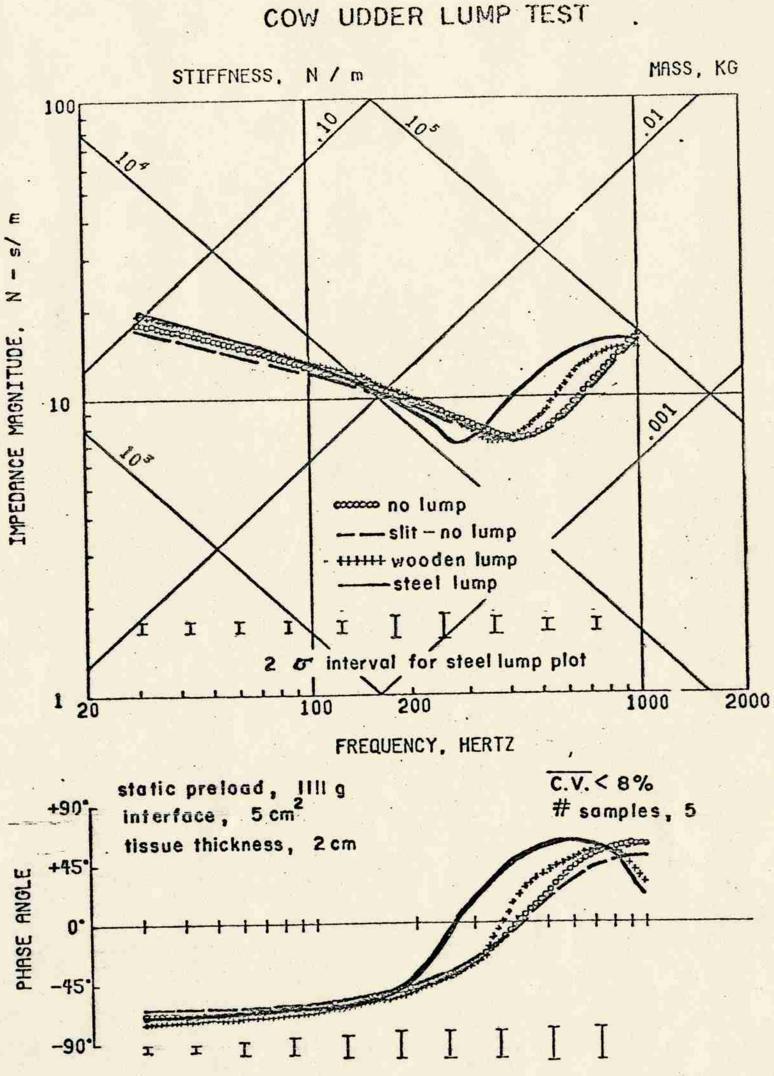

Figure 5 Means from 5 lump tests on 2 cm thick tissue for steel and wooden lumps weighing 8 and 1 g, respectively

located above, below, medially and laterally from the nipple at a distance of three centimeters. In addition, if the subject knew of any cystic lumps, they were located and tested along with the bilaterally symetrical position on the other breast.

Although in vivo tissue thickness could only be estimated, the sample thickness was found to be the most important factor in determining the nature of the impedance plot. As tissue thickness increased, however, the in vivo tissue showed a different response from that noted in the cow udder tissue. In the cow tissue, with increasing tissue thickness, the impedance magnitude for the lower frequencies (below 200 Hz) decreased. In human tissue, the thicker samples plots tend to have less inflection and higher impedance magnitude values, Figure 6. An earlier set of experiments on goat's udders, in vivo, showed the same effect. This may represent the differences associated with the higher concentration of fluid in the in vivo versus the in vitro state.

Figure 6 shows two lump tests for women reporting cystic lumps. The lower magnitude curve shows the most dramatic difference between the lump condition and the no lump condition. Although the actual impedance values are very nearly the same, and there are no apparent additional resonances or antiresonances, in the lump plot, the lump curve shape has somewhat more pronounced inflections. The upper curves, however, are more typical of the lump test results among women reporting cystic lumps. No significant differences was noted at any frequency for either of the lump tests.

A Lumped Parameter Model for Mammary Tissue

Unless impedance plots like those already shown can be related to the physical characteristics of the tissue and then normalized for certain sets of conditions, they are of limited use in understanding the behavior of a tissue system. By trial and

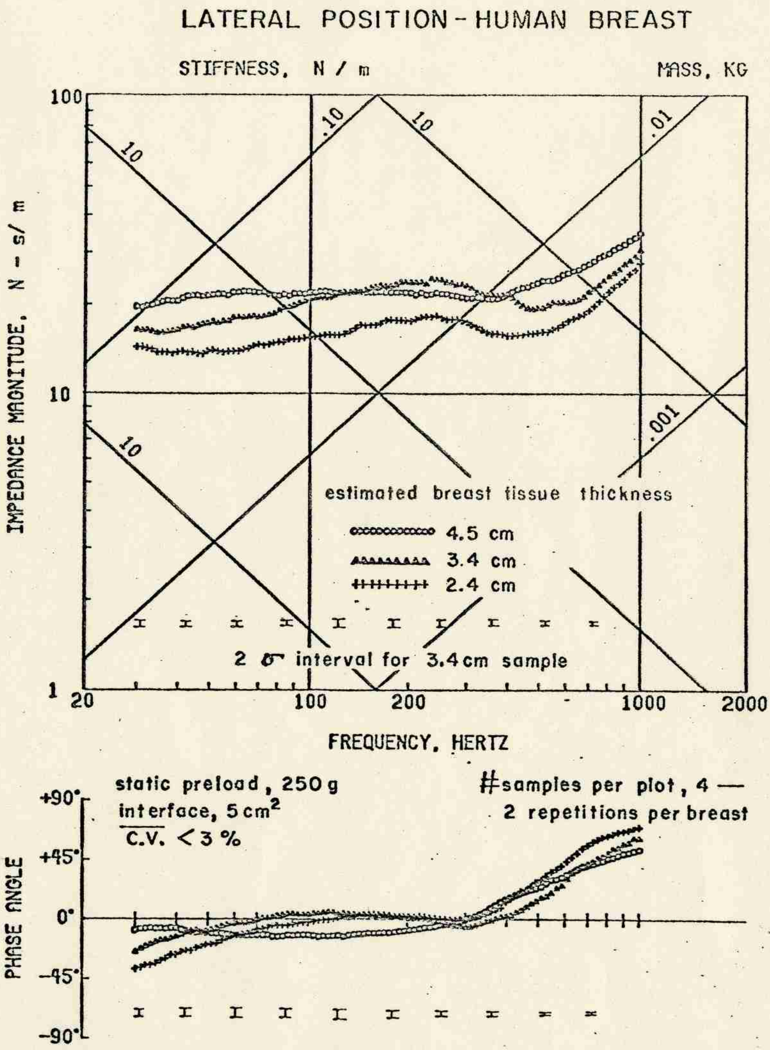

Figure 8 Lateral test position from large, medium and small breasted women

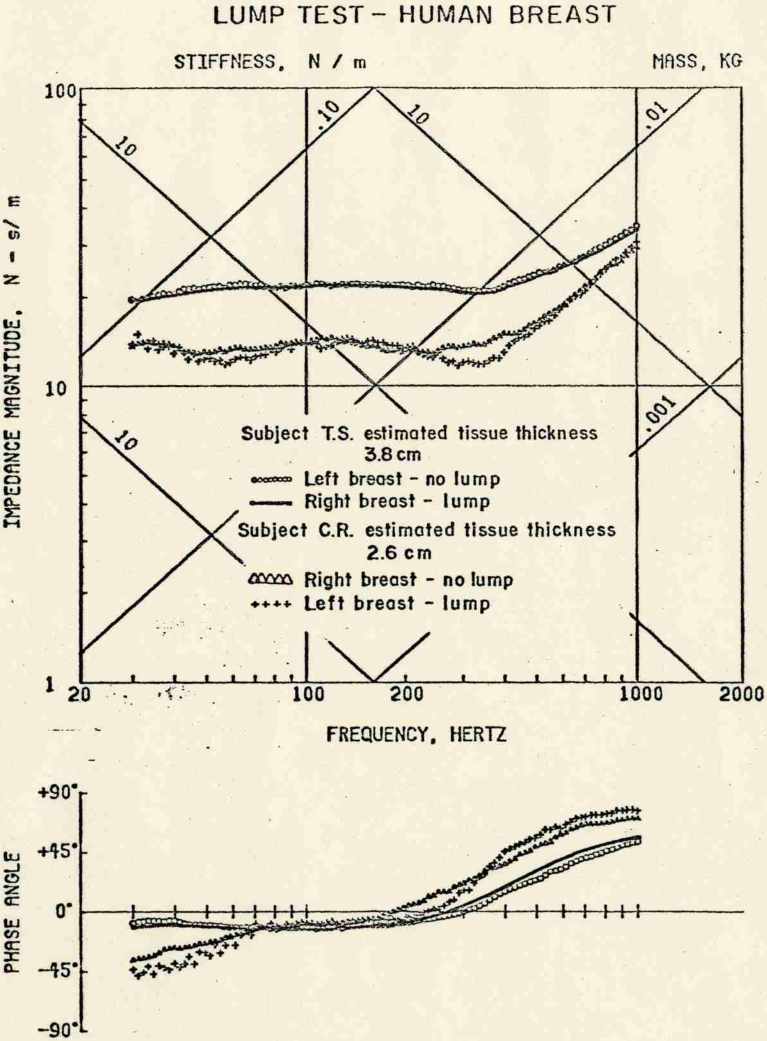

Figure 7 Impedance test on two women reporting palpable cystic lumps

error it was found that the transfer function describing the six element mechanical network of Figure 8 also generally conforms to the observed mechanical impedance data. The model equation is

$$Z = (wm_1)_i + \frac{1}{1/(C_1 - (\frac{K_1}{w})i) + 1/(C_2 + (M_2 w - \frac{K_2}{w})i)} \qquad \text{Eq. 2}$$

Then using a parameter fitting computer program, the model was optimized for the magnitude curves of selected impedance plots. Since best fit solutions are not unique, the closeness of fit for the phase curve as well as the reasonableness of the values was used as a measure of the quality of the model. The model fit was extremely good for all animal tissue data, Figure 9.

In order to evaluate the potential of driving point mechanical impedance for locating and characterizing lumps within soft tissue, the six element model was applied to the foam rubber lump test plots. These were chosen because they show the most dramatic difference between the 'with lump' and 'without lump' condition. It was found that the six element model fit the 'with lump' condition almost as well as the without lump condition, Figure 14. The largest difference in the parameter values, as would be expected, is in m_2 which increases according to the mass of the lump and k_2 which increases slightly, probably because of the additional strain in the region of the rigid lump. In terms of the real system, this would tend to indicate that the lump does not resonate significantly independently from the surrounding tissue. Careful scrutiny of the foam rubber lump test plots indicate the presence of at least three independently resonating masses. This indicates a nine element model and although several were tried, none were found to yield reasonable parameters or a closer fit to the observed data. Note, however, no presumption of non existance of such a model should be made on one failure to find it.

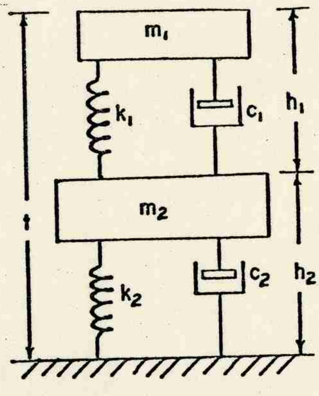

Figure ~~9.1~~ 8 Physical model of soft mammary tissue used in developing predictive equation for mechanical impedance plots

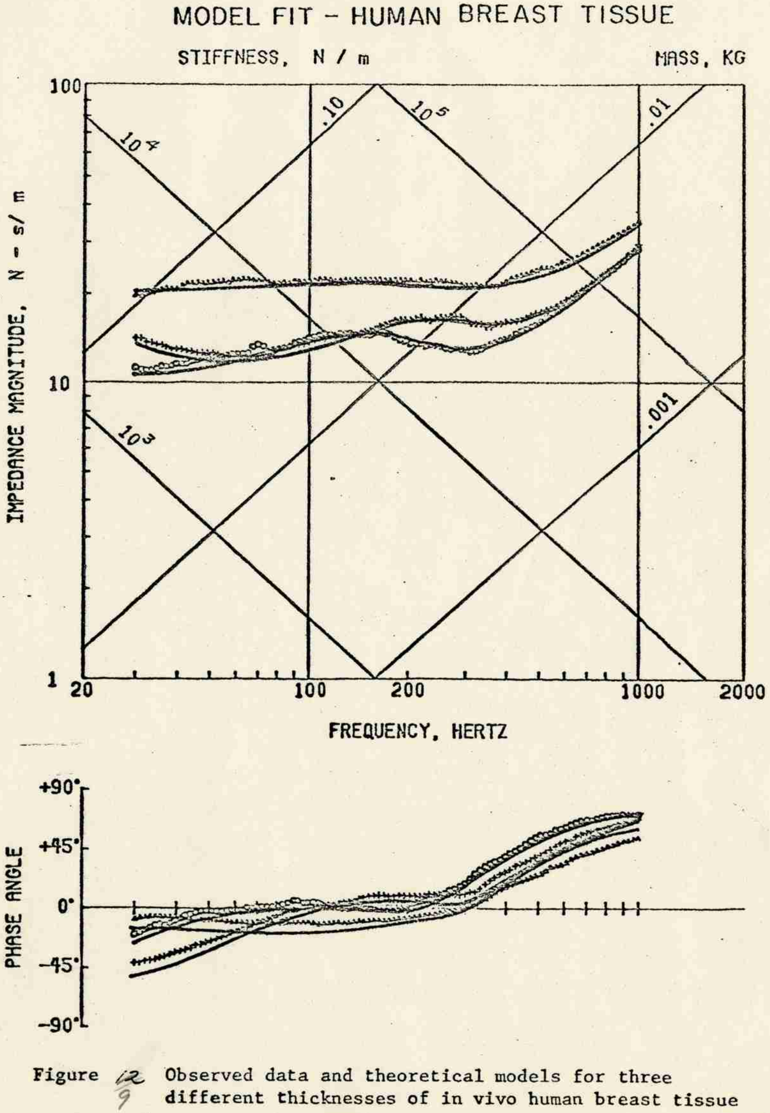

Figure ~~12~~ 9 Observed data and theoretical models for three different thicknesses of in vivo human breast tissue

Conclusion

Although neoplasms are not significantly different in specific gratity from normal tissue it was felt that their presence might be detected by vibratory methods. This study, however, indicated that mechanical impedance is not a feasible breast cancer tumor detecting technique because the lumps tend to vibrate with the embedding tissue. The findings, however, are not conclusive and many questions should be answered before discounting the technique's use. For further investigation, the region above 1000 Hz and below 30 Hz may show significant effects. Tests on in vivo breast tissue in women with confirmed carcinomas would be a more direct indication of diagnostic possibilities. Other suggestions include development of better, more complex models, surgical emplantation of artificial lumps in animals for testing and the use of several transducers for locating abnormalities or lumps.

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