FIG. 1

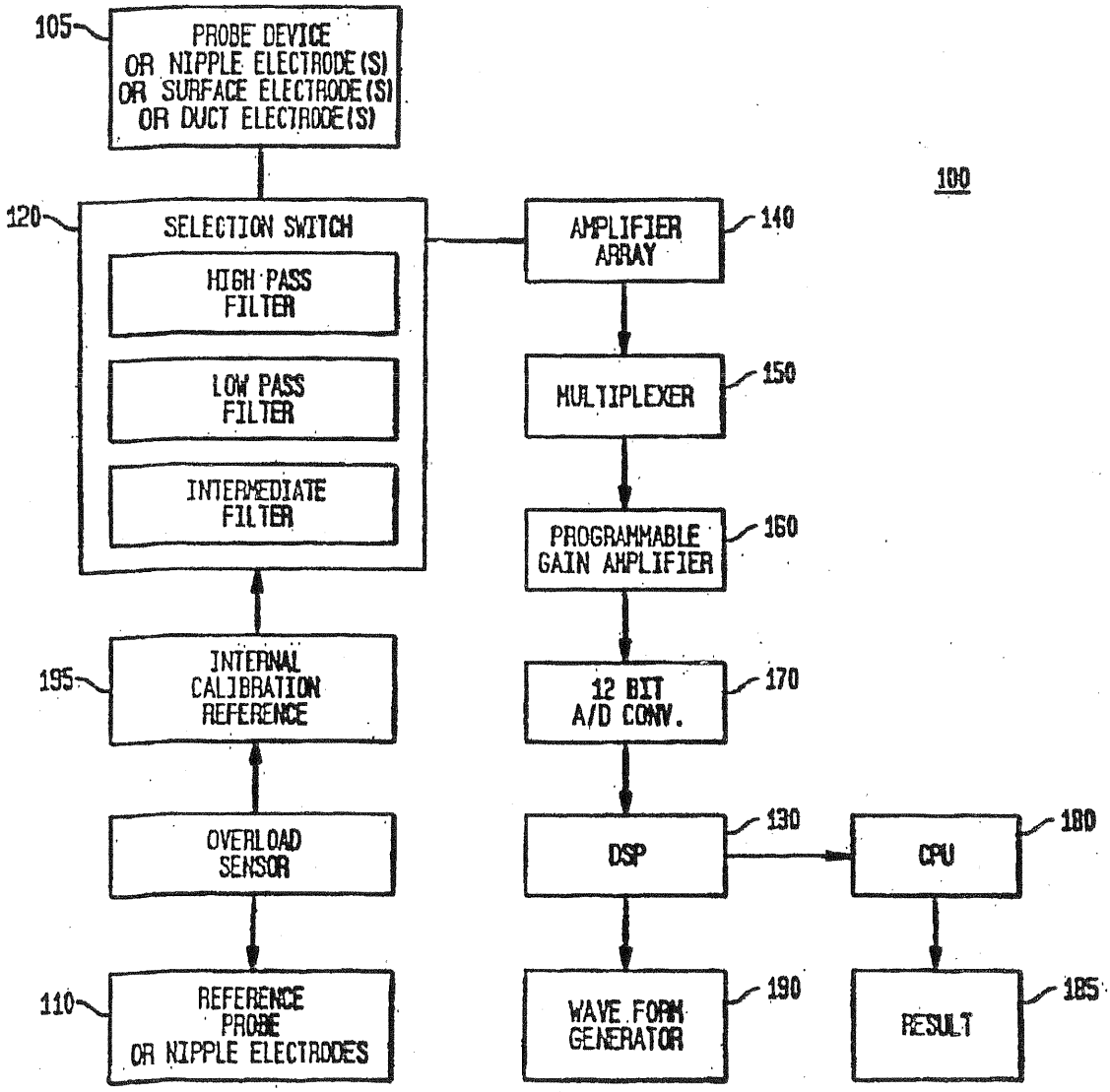

105
PROBE DEVICE OR NIPPLE ELECTRODE(S) OR SURFACE ELECTRODE(S) OR DUCT ELECTRODE(S)
100
120
SELECTION SWITCH
HIGH PASS FILTER
LOW PASS FILTER
INTERMEDIATE FILTER
140
AMPLIFIER ARRAY
150
MULTIPLEXER
160
PROGRAMMABLE GAIN AMPLIFIER
170
12 BIT A/D CONV.
130
DSP
180
CPU
195
INTERNAL CALIBRATION REFERENCE
OVERLOAD SENSOR
110
REFERENCE PROBE OR NIPPLE ELECTRODES
190
WAVE FORM GENERATOR
185
RESULT

FIG. 2

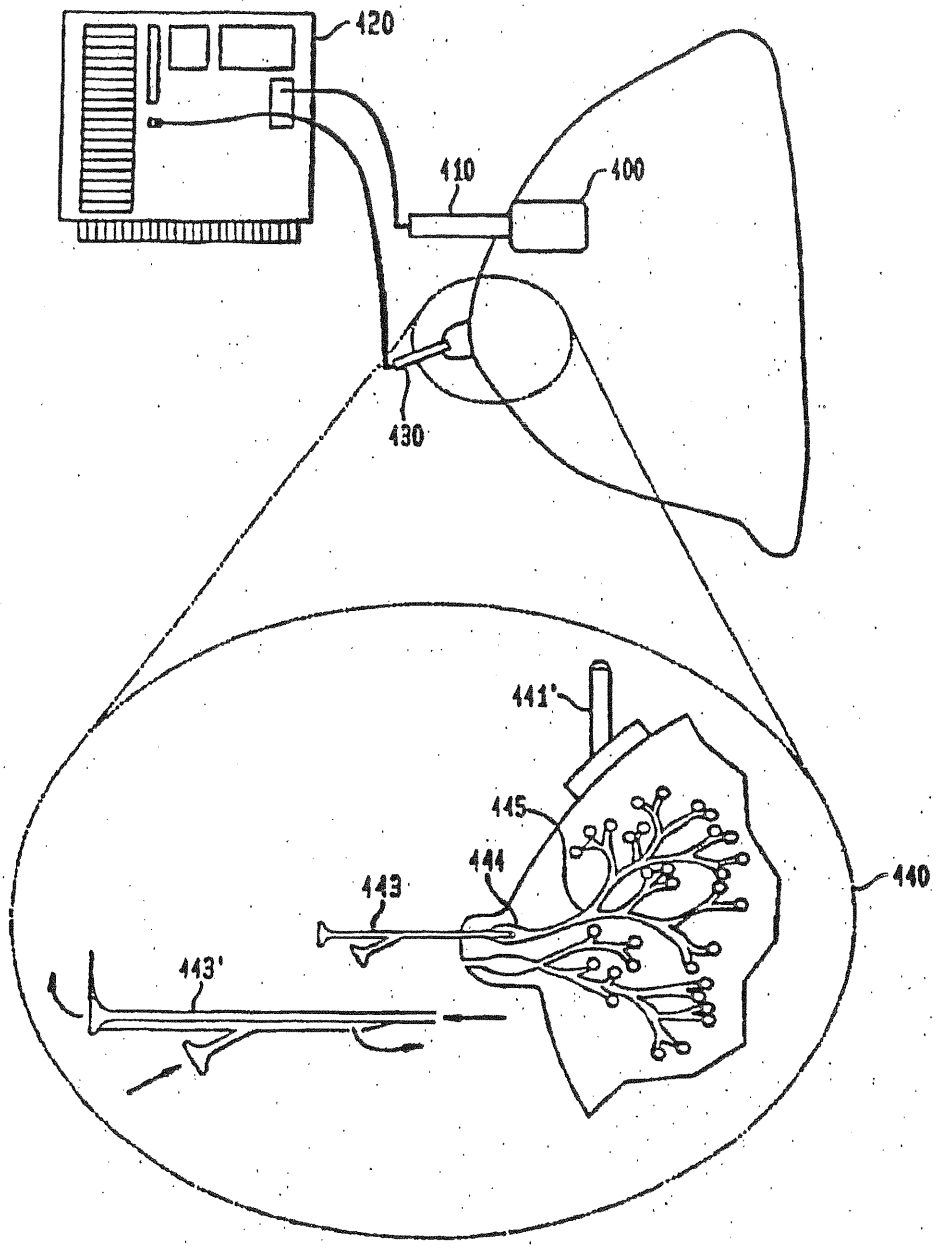


FIG. 3

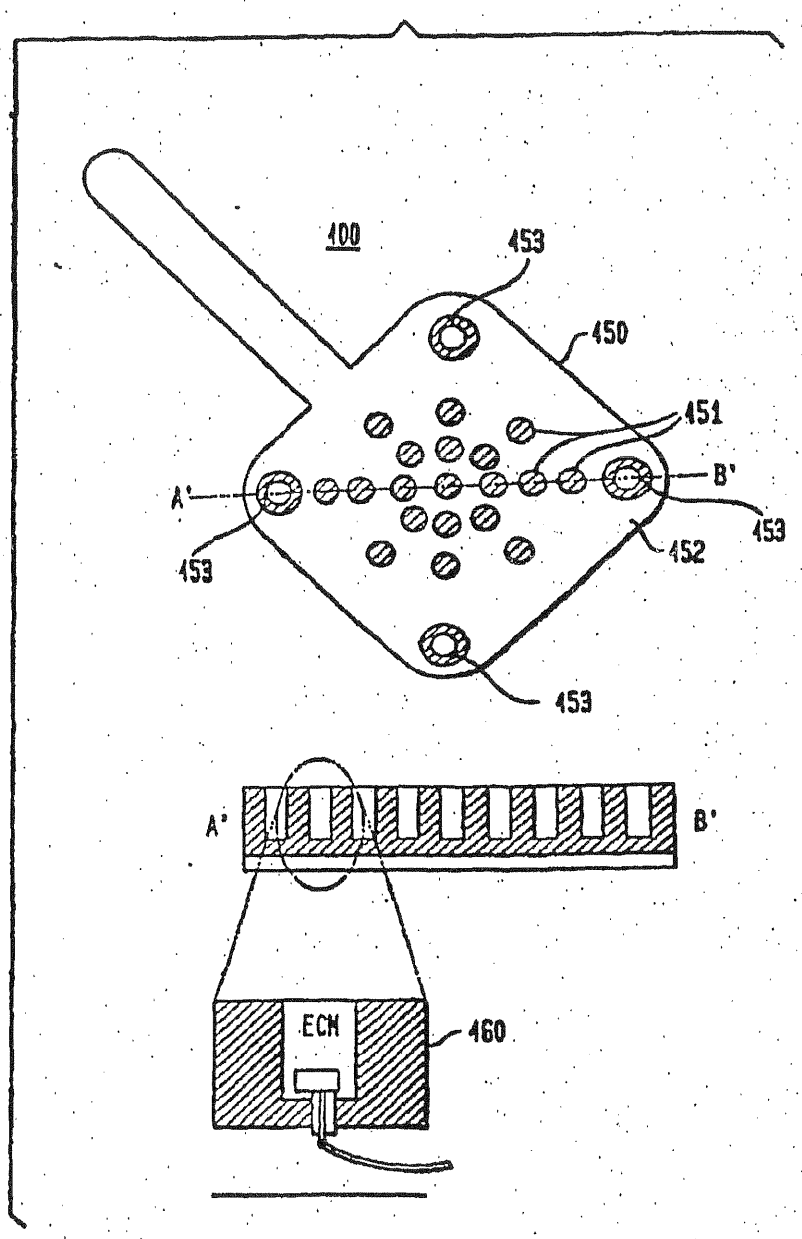


FIG. 4

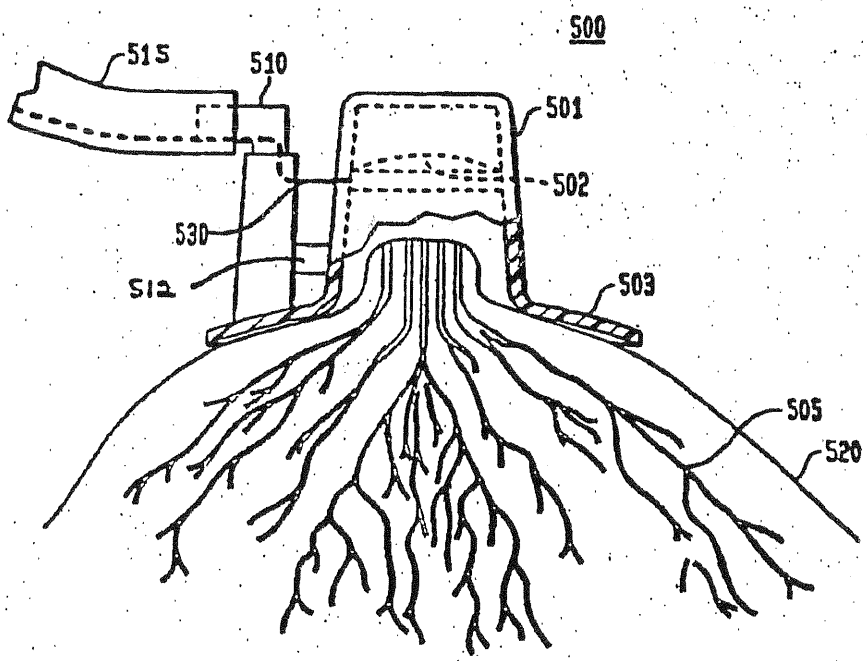


FIG. 5

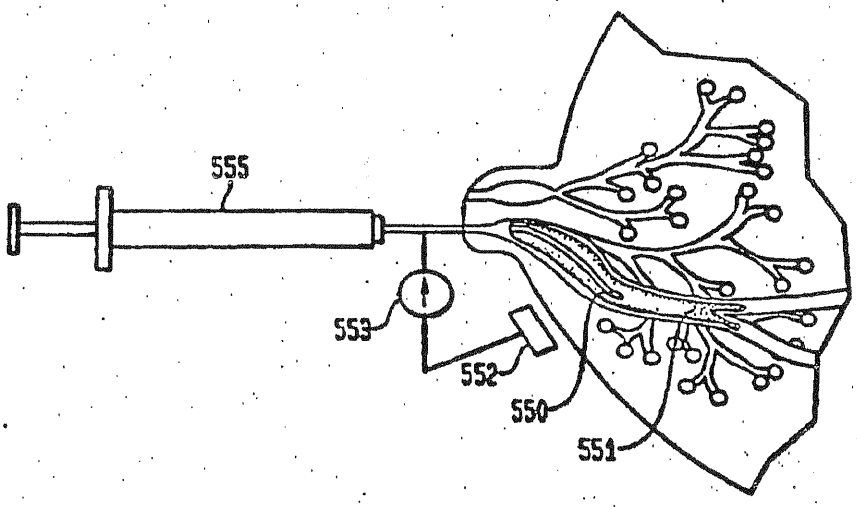


FIG. 6

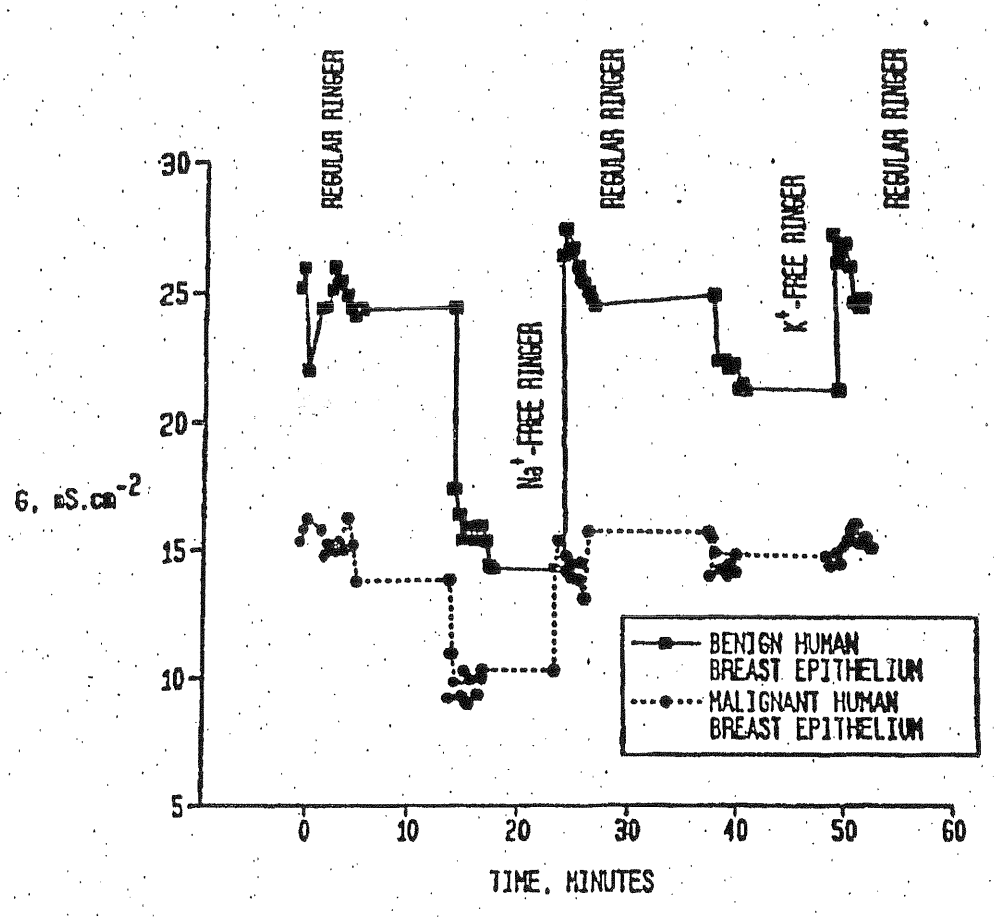

REGULAR RINGER
Na+-FREE RINGER
REGULAR RINGER
K+-FREE RINGER
REGULAR RINGER
G, mS.cm-2
30
25
20
15
10
5
0
10
20
30
40
50
60
TIME, MINUTES
BENIGN HUMAN BREAST EPITHELIUM
MALIGNANT HUMAN BREAST EPITHELIUM

FIG. 7

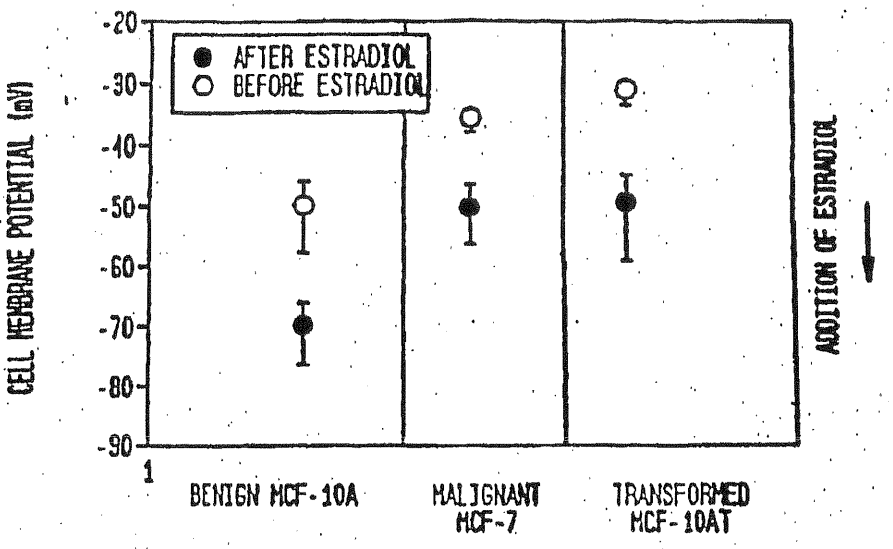

-20
-30
-40
-50
-60
-70
-80
-90
AFTER ESTRADIOL
BEFORE ESTRADIOL
CELL MEMBRANE POTENTIAL (mV)
ADDITION OF ESTRADIOL
1
BENIGN MCF-10A
MALIGNANT MCF-7
TRANSFORMED MCF-10AT

FIG. 8

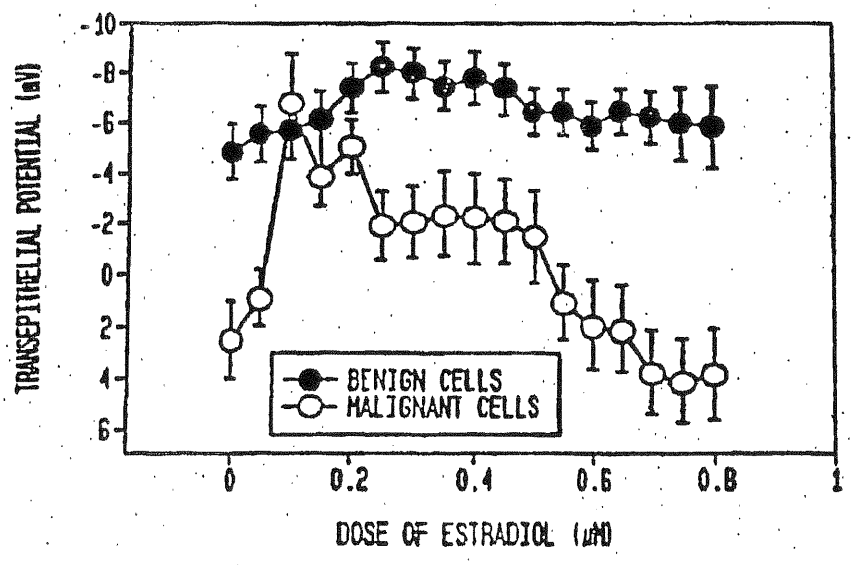

-10
-8
-6
-4
-2
0
2
4
6
TRANSEPITHELIAL POTENTIAL (mV)
BENIGN CELLS
MALIGNANT CELLS
0
0.2
0.4
0.6
0.8
1
DOSE OF ESTRADIOL (μM)

FIG. 9

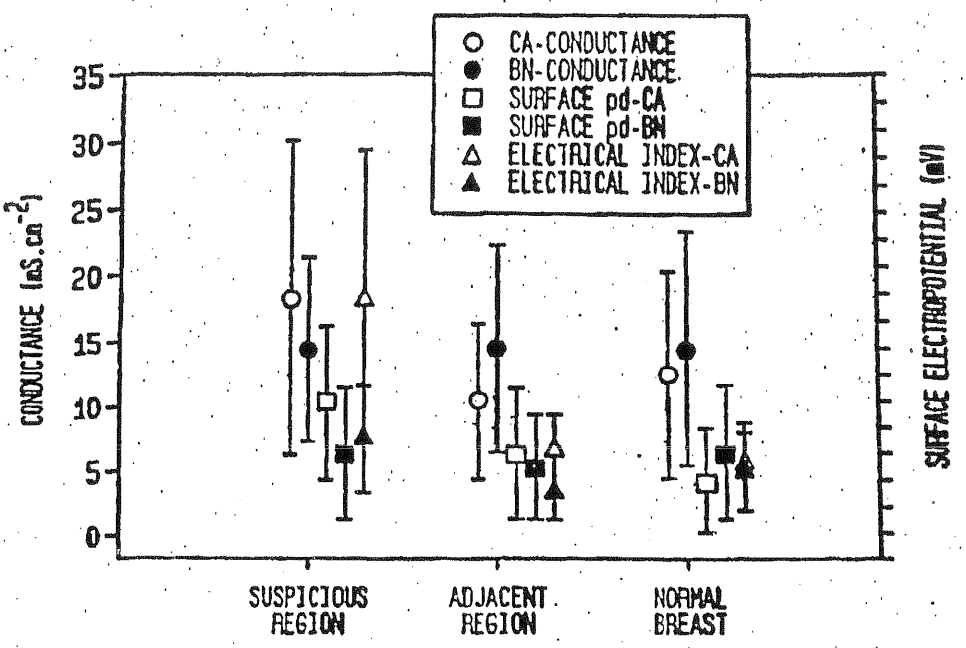

CA-CONDUCTANCE
BN-CONDUCTANCE
SURFACE pd-CA
SURFACE pd-BN
ELECTRICAL INDEX-CA
ELECTRICAL INDEX-BN
CONDUCTANCE (mS.cm^{-2})
SURFACE ELECTROPOTENTIAL (mV)
35
30
25
20
15
10
5
0
SUSPICIOUS REGION
ADJACENT REGION
NORMAL BREAST

FIG. 10

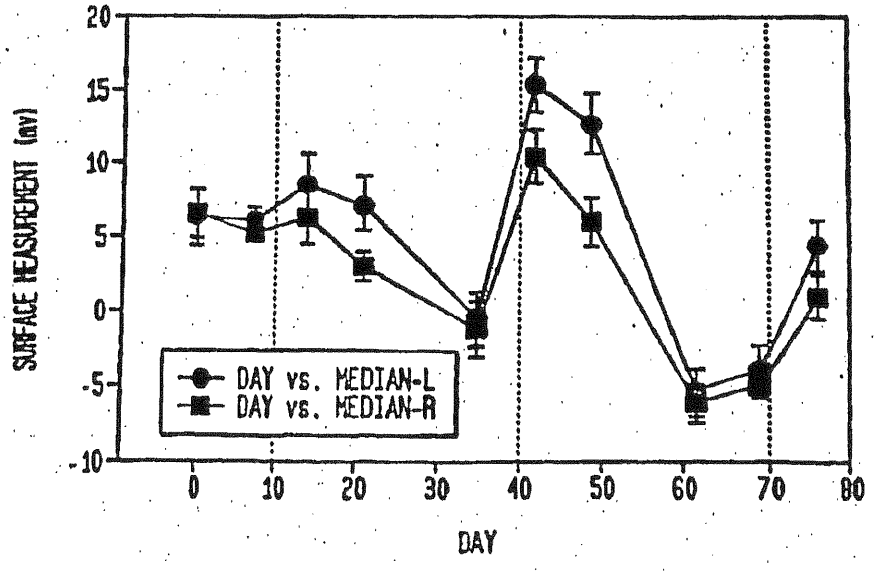

SURFACE MEASUREMENT (mv)
DAY
DAY vs. MEDIAN-L
DAY vs. MEDIAN-R
20
15
10
5
0
-5
-10
0
10
20
30
40
50
60
70
80

FIG. 11

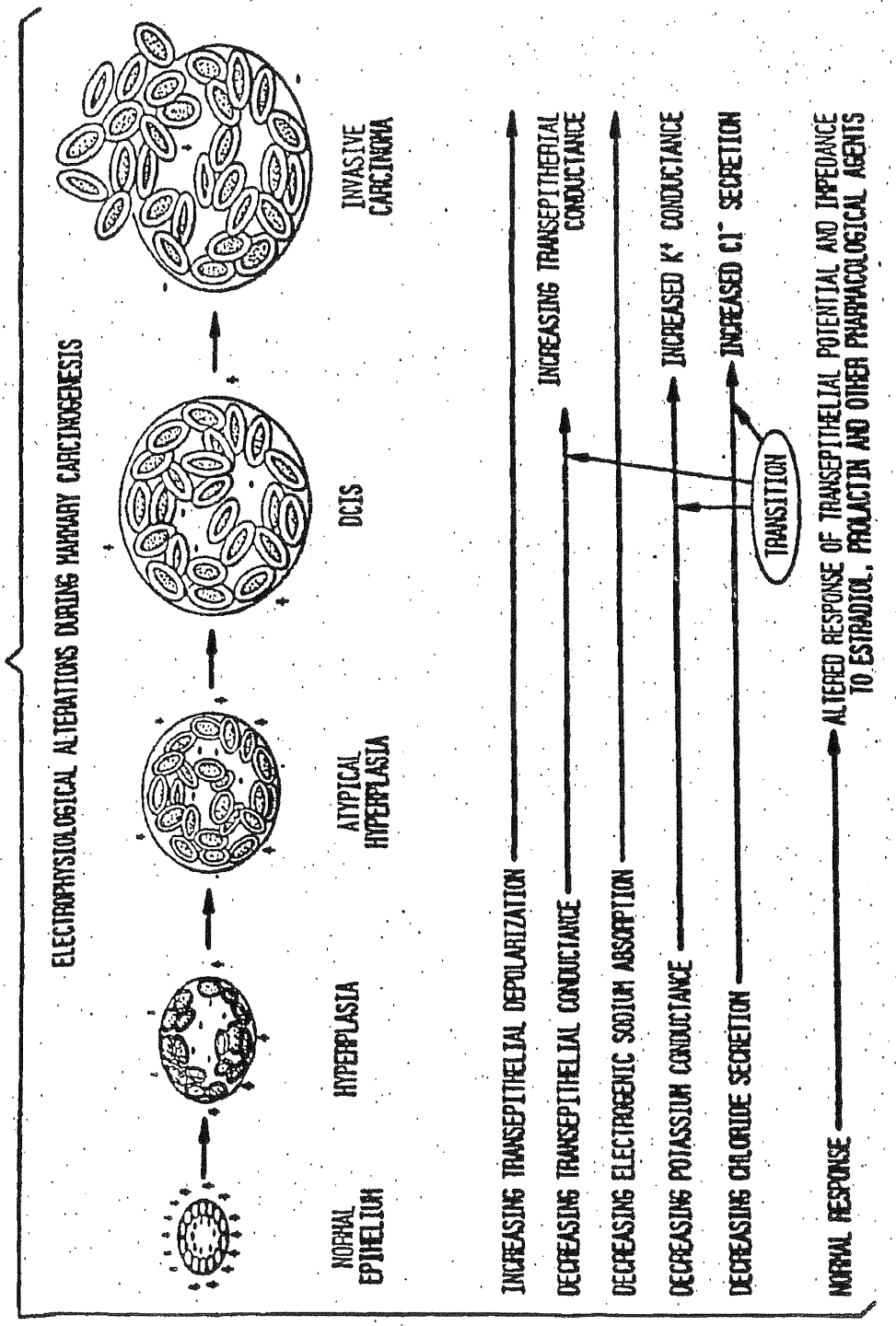

ELECTROPHYSIOLOGICAL ALTERATIONS DURING MAMMARY CARCINOGENESIS
NORMAL EPITHELIUM
HYPERPLASIA
ATYPICAL HYPERPLASIA
DCIS
INVASIVE CARCINOMA
INCREASING TRANSEPITHELIAL DEPOLARIZATION
DECREASING TRANSEPITHELIAL CONDUCTANCE
INCREASING TRANSEPITHERIAL CONDUCTANCE
DECREASING ELECTROGENIC SODIUM ABSORPTION
DECREASING POTASSIUM CONDUCTANCE
INCREASED K+ CONDUCTANCE
DECREASING CHLORIDE SECRETION
INCREASED Cl- SECRETION
TRANSITION
NORMAL RESPONSE
ALTERED RESPONSE OF TRANSEPITHELIAL POTENTIAL AND IMPEDANCE TO ESTRADIOL, PROLACTIN AND OTHER PHARMACOLOGICAL AGENTS

FIG. 12

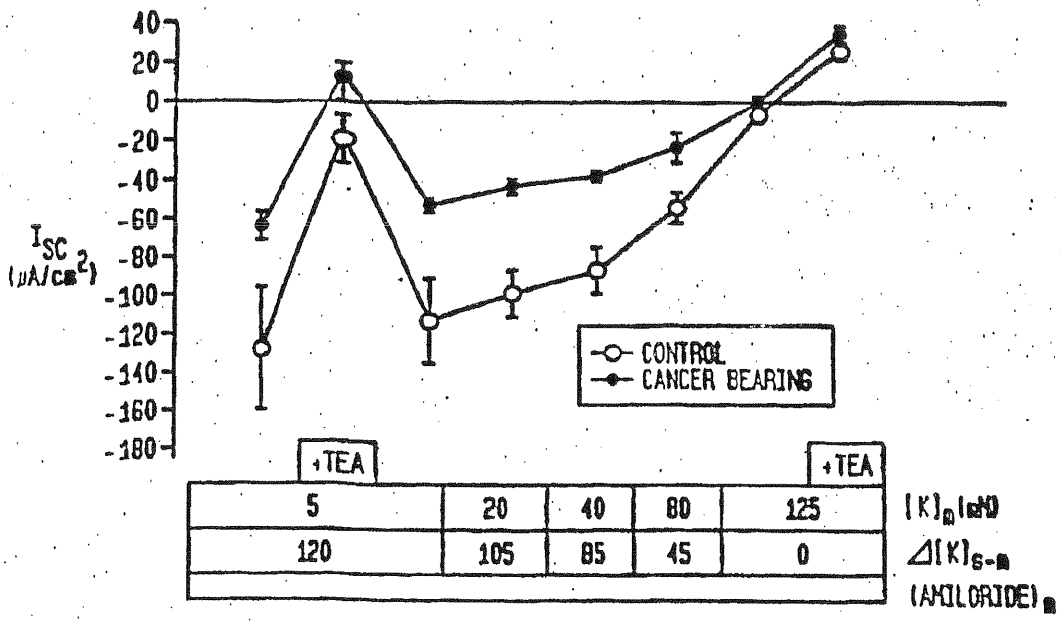

40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
I_{SC} ($\mu A/cm^2$)
CONTROL
CANCER BEARING
+TEA
+TEA
5
20
40
80
125
$[K]_m$ (mM)
120
105
85
45
0
$\Delta[K]_{s-m}$
(AMILORIDE)$_m$

FIG. 13

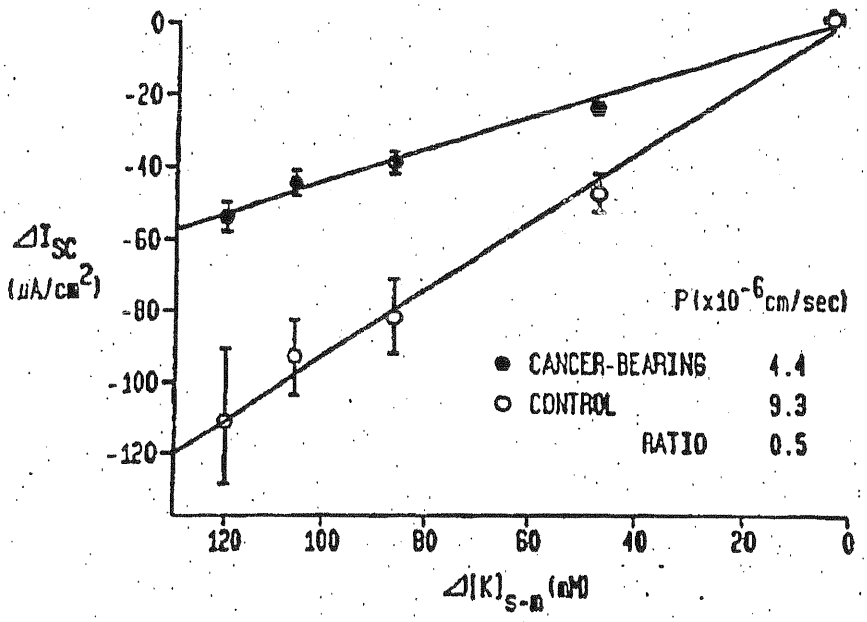

0
-20
-40
-60
-80
-100
-120
ΔISC
(μA/cm2)
P(x10-6cm/sec)
CANCER-BEARING 4.4
CONTROL 9.3
RATIO 0.5
120
100
80
60
40
20
0
Δ[K]S-M (mM)

FIG. 14

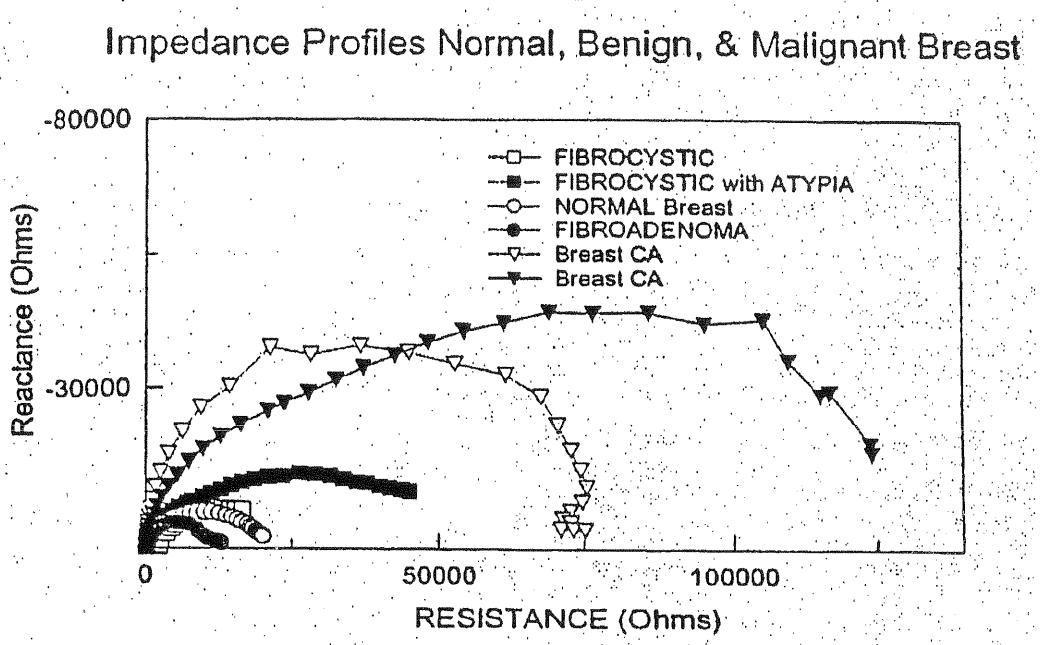

Impedance Profiles Normal, Benign, & Malignant Breast
-80000
-30000
Reactance (Ohms)
FIBROCYSTIC
FIBROCYSTIC with ATYPIA
NORMAL Breast
FIBROADENOMA
Breast CA
Breast CA
0
50000
100000
RESISTANCE (Ohms)

FIG. 15

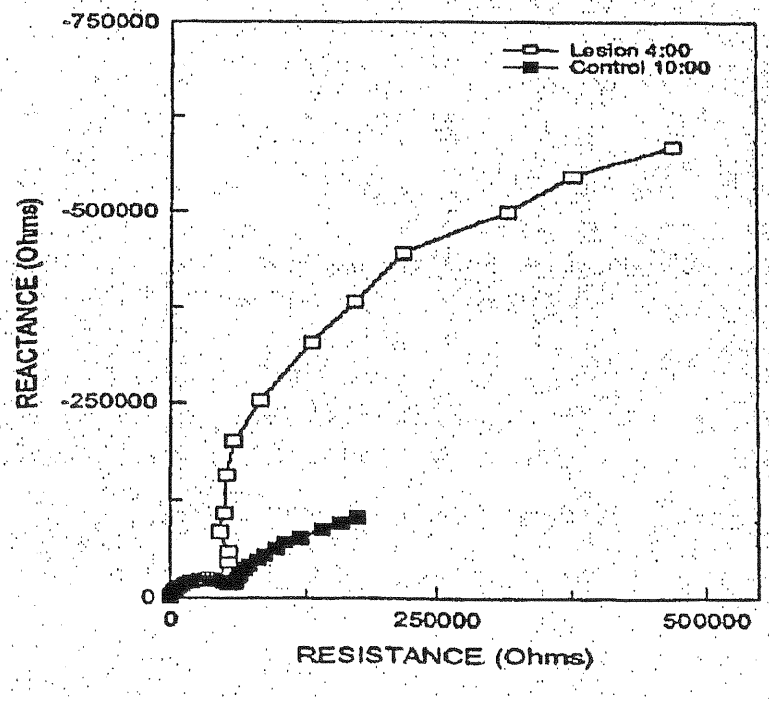

-750000
-500000
-250000
0
REACTANCE (Ohms)
Lesion 4:00
Control 10:00
0
250000
500000
RESISTANCE (Ohms)

FIG. 16

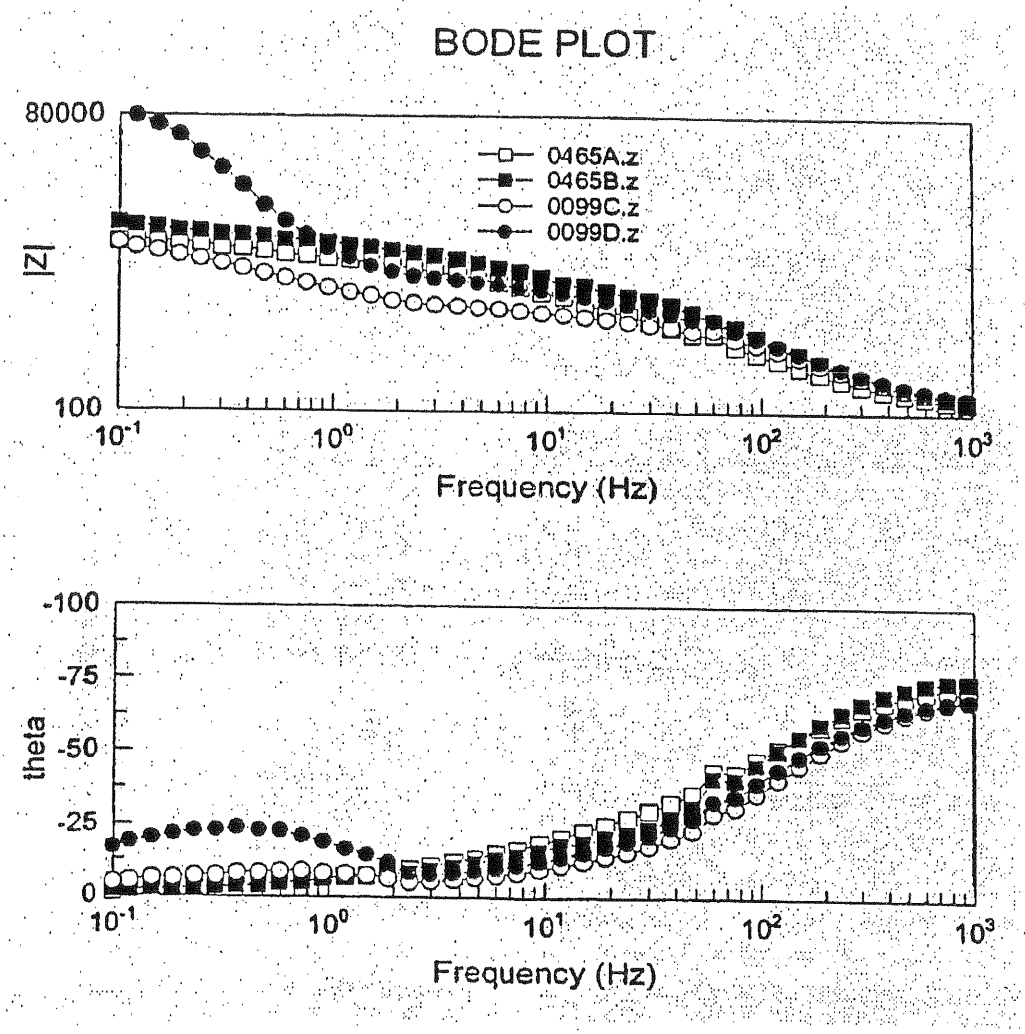

BODE PLOT
80000
100
|Z|
0465A.z
0465B.z
0099C.z
0099D.z
10-1
100
101
102
103
Frequency (Hz)
-100
-75
-50
-25
0
theta
10-1
100
101
102
103
Frequency (Hz)

FIG. 17

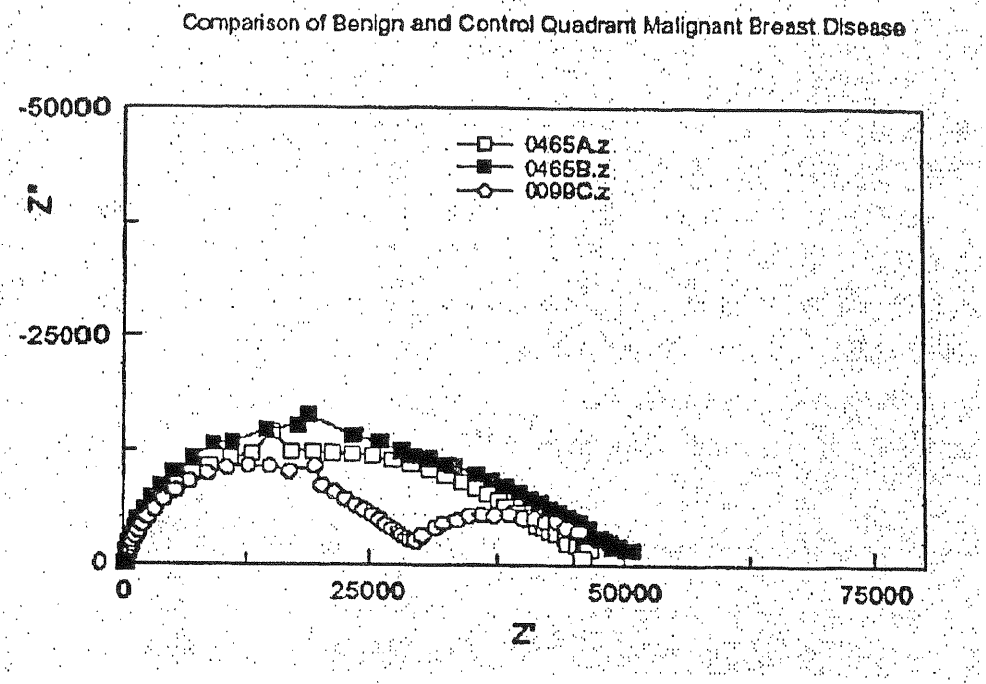

Comparison of Benign and Control Quadrant Malignant Breast Disease
-50000
-25000
0
Z"
0
25000
50000
75000
Z'
0465A.z
0465B.z
0099C.z

FIG. 18

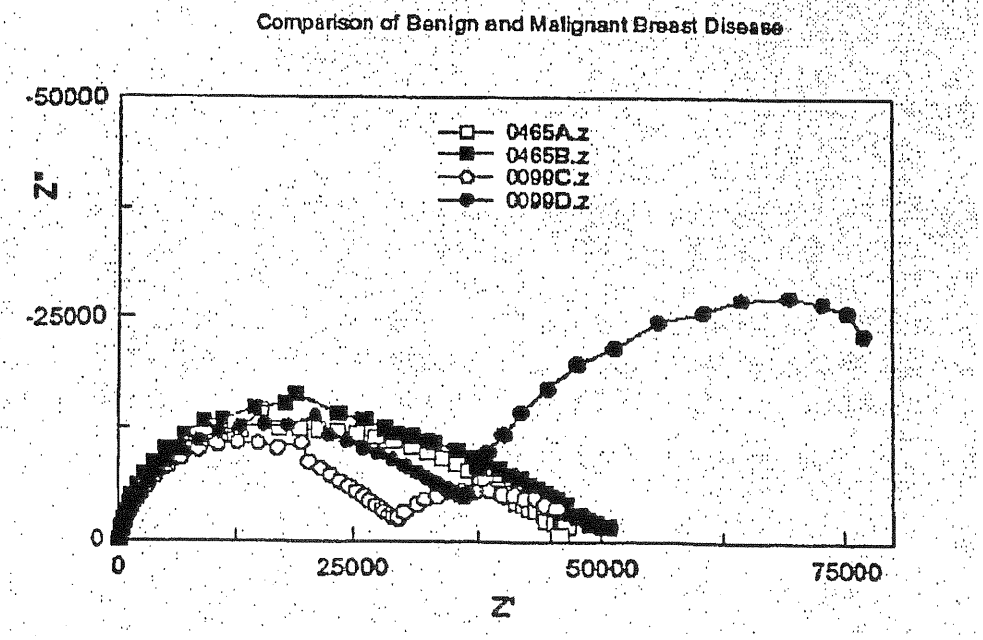

Comparison of Benign and Malignant Breast Disease
-50000
-25000
0
Z"
0
25000
50000
75000
Z'
0465A.z
0465B.z
0099C.z
0099D.z

FIG. 19

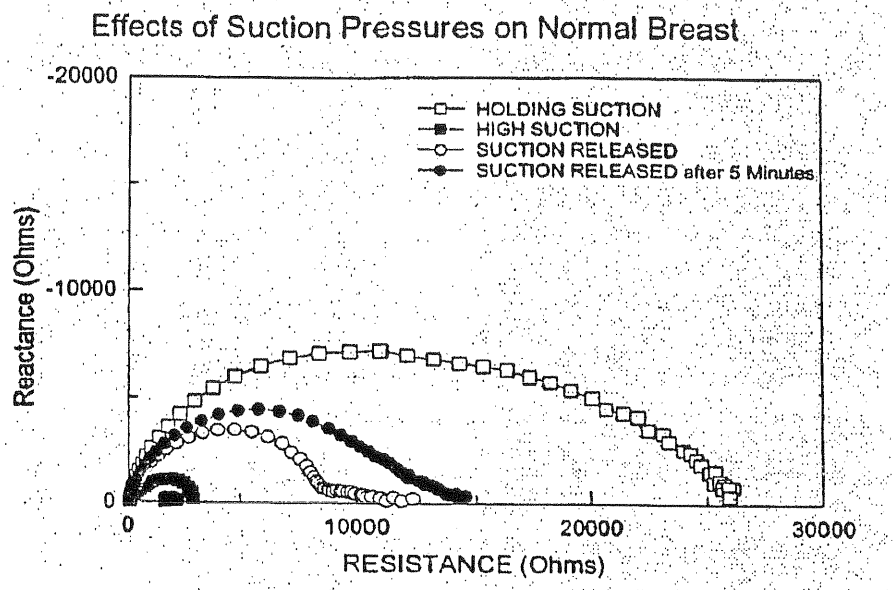

Effects of Suction Pressures on Normal Breast
-20000
-10000
0
Reactance (Ohms)
HOLDING SUCTION
HIGH SUCTION
SUCTION RELEASED
SUCTION RELEASED after 5 Minutes
0
10000
20000
30000
RESISTANCE (Ohms)

FIG. 20

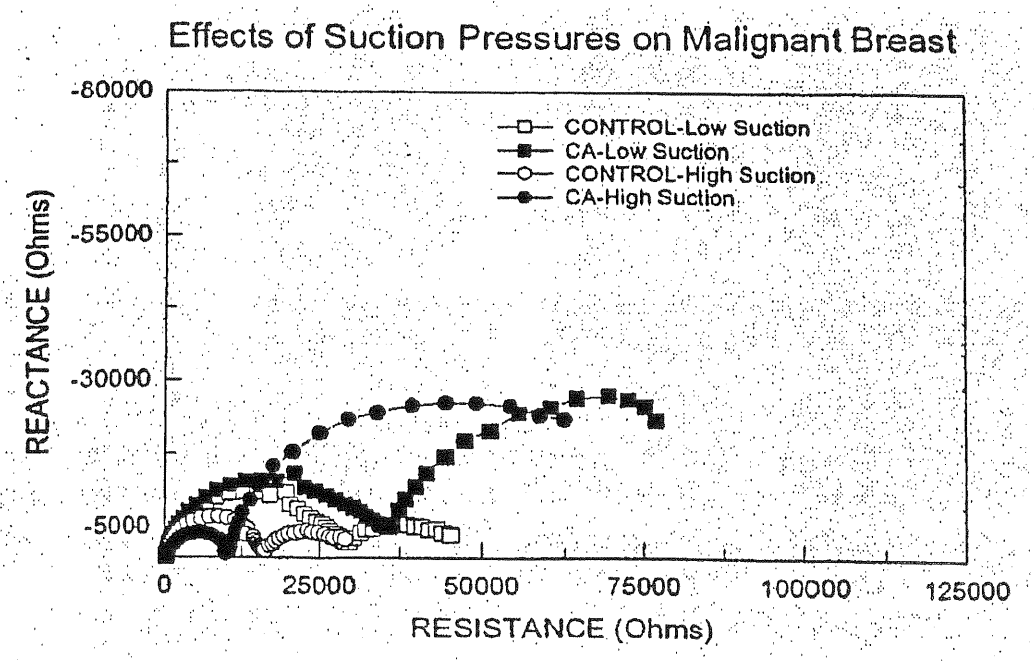

Effects of Suction Pressures on Malignant Breast
-80000
-55000
-30000
-5000
REACTANCE (Ohms)
CONTROL-Low Suction
CA-Low Suction
CONTROL-High Suction
CA-High Suction
0
25000
50000
75000
100000
125000
RESISTANCE (Ohms)

FIG. 21

Impedance Estimation Method
Applied to Data of Figure 20

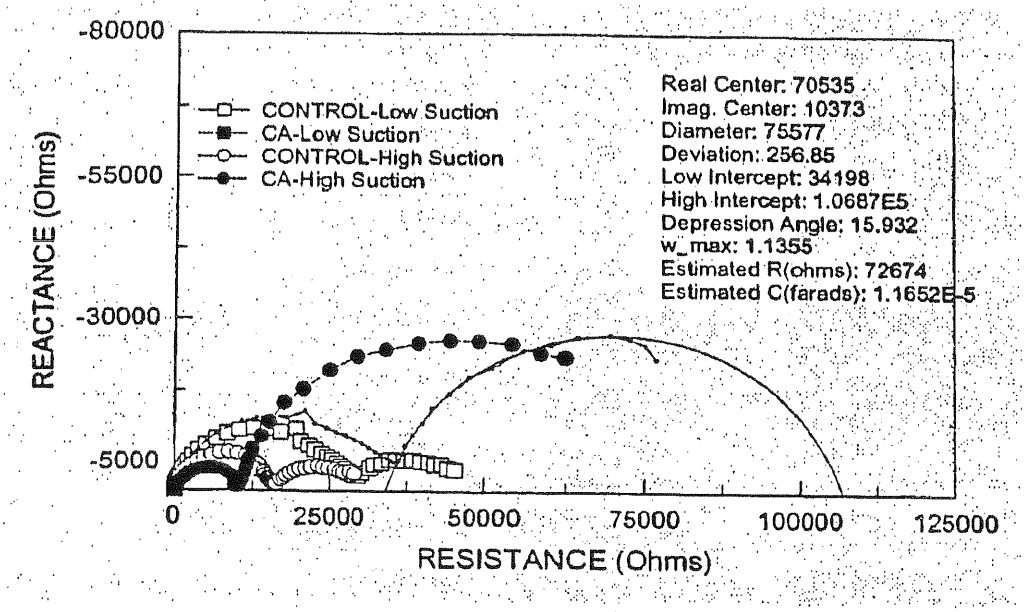
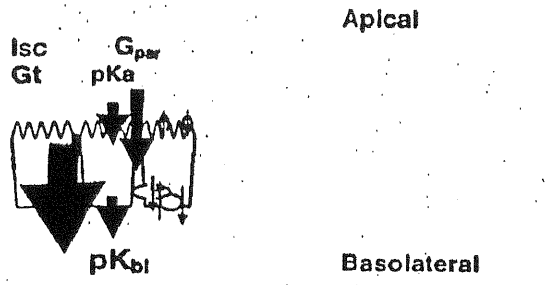
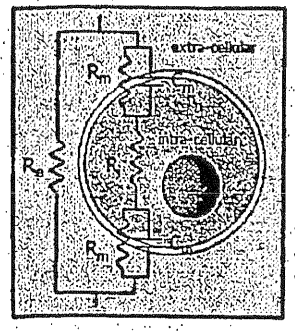


Figure 22-1A



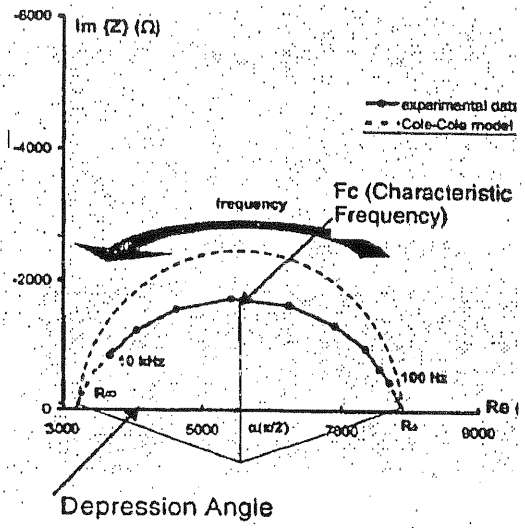
Electrical Pathways across Breast Epithelium

Fig. 22-1B



Electrical Modeling
of Breast Epithelium

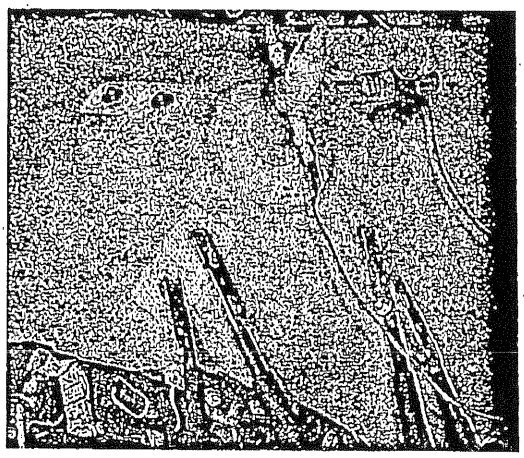
Fig. 22-1C



Nyquist Plot Using Variable Frequency Sine Wave

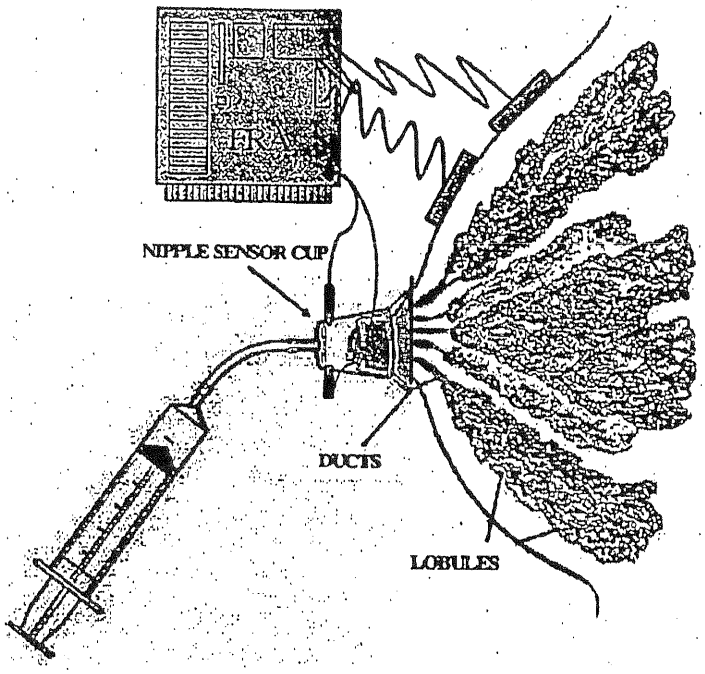
Epithelial Impedance
Spectroscopy

Figure 22-1D



Measurement Set-up and Nipple Sensor Cup

Figure 22-2A



Representation of Measurement Set-up

Figure 22-2B

Epithelial Impedance Plot - Normal Subject

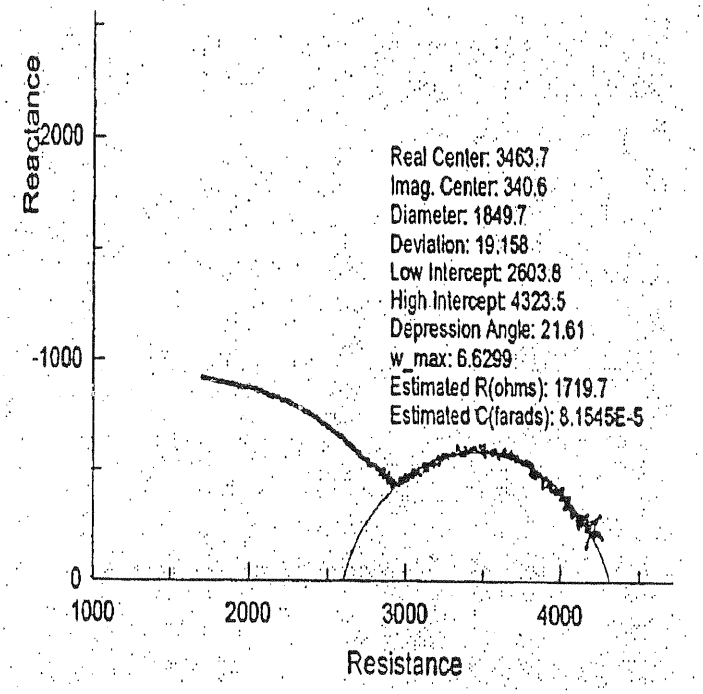


Figure 22-2C

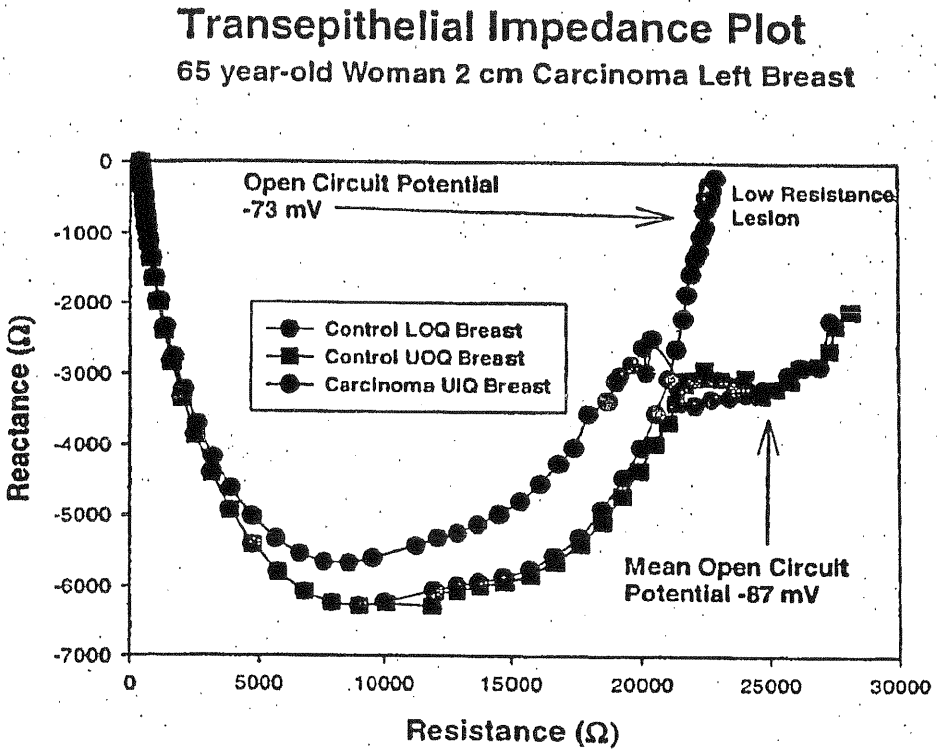

Transepithelial Impedance Plot
65 year-old Woman 2 cm Carcinoma Left Breast
Open Circuit Potential
-73 mV
Low Resistance
Lesion
Control LOQ Breast
Control UOQ Breast
Carcinoma UIQ Breast
Mean Open Circuit
Potential -87 mV
Reactance (Ω)
Resistance (Ω)
0
-1000
-2000
-3000
-4000
-5000
-6000
-7000
0
5000
10000
15000
20000
25000
30000

Figure 22-2D

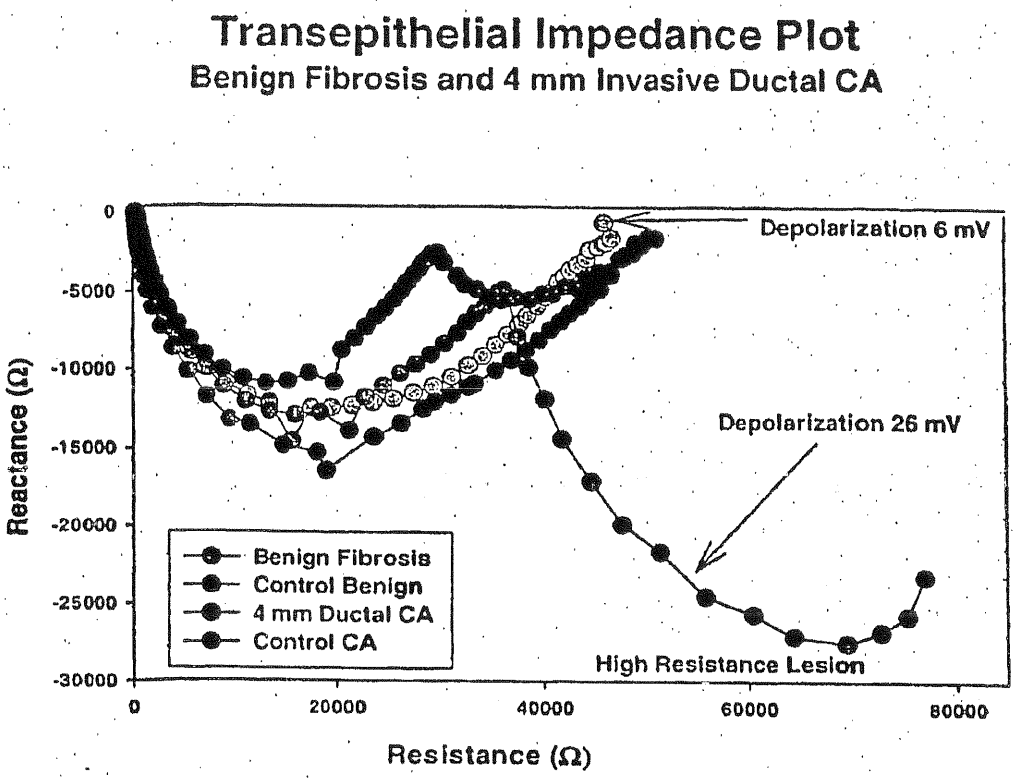

Transepithelial Impedance Plot
Benign Fibrosis and 4 mm Invasive Ductal CA
Depolarization 6 mV
Depolarization 26 mV
High Resistance Lesion
Benign Fibrosis
Control Benign
4 mm Ductal CA
Control CA
Reactance (Ω)
Resistance (Ω)
0
-5000
-10000
-15000
-20000
-25000
-30000
0
20000
40000
60000
80000

Figure 22-3A

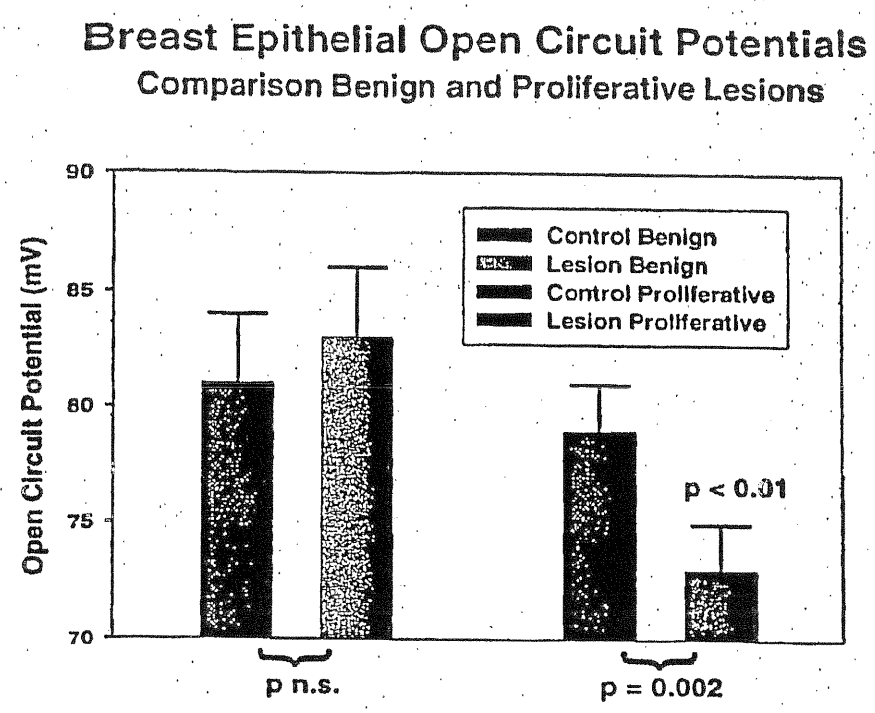
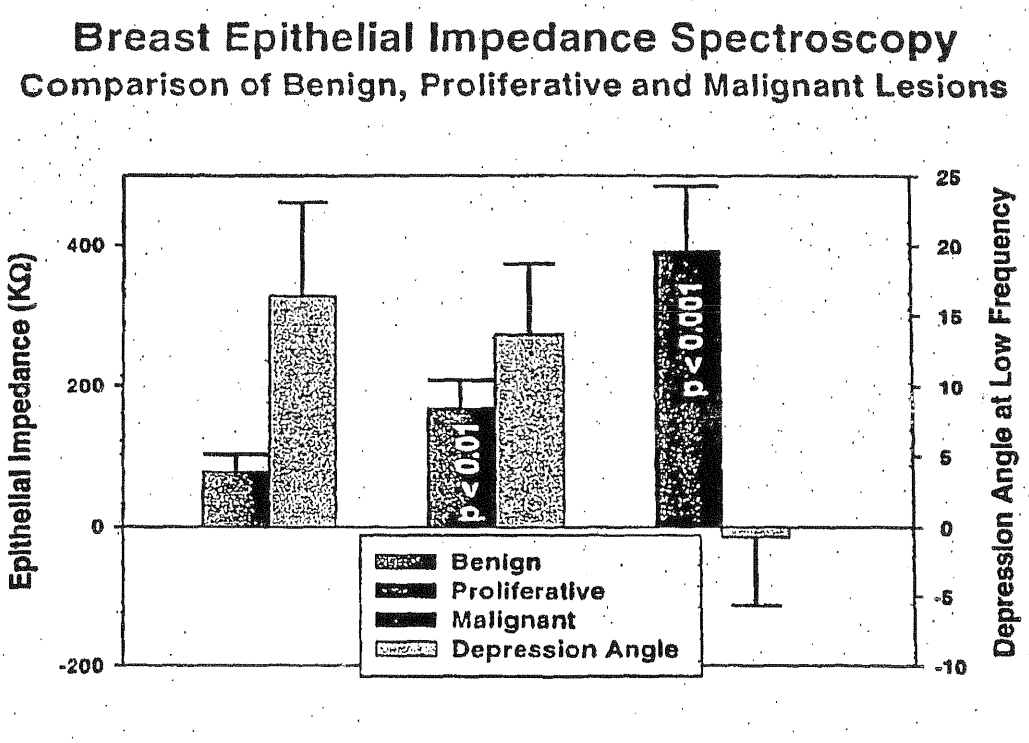

Breast Epithelial Open Circuit Potentials
Comparison Benign and Proliferative Lesions
Open Circuit Potential (mV)
90
85
80
75
70
Control Benign
Lesion Benign
Control Proliferative
Lesion Proliferative
p < 0.01
p n.s.
p = 0.002

Figure 22-3B


Breast Epithelial Impedance Spectroscopy
Comparison of Benign, Proliferative and Malignant Lesions
Epithelial Impedance (KΩ)
400
200
0
-200
25
20
15
10
5
0
-5
-10
Depression Angle at Low Frequency
p < 0.01
p < 0.001
Benign
Proliferative
Malignant
Depression Angle