ULTRASOUND VELOCITY IN CERVIX UTERI IN CORRELATION WITH STRUCTURAL CHANGES FOR DIAGNOSIS OF INCOMPETENCE

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The diagnosis of cervical incompetence can be achieved by evaluating the clinical history of multigravid patients. If the typical history of incompetence is not noted, the clinician may rely on observing the appearance of symptoms which are usually observed late in the course of this condition. The condition is more complex for multigravid patients with congenital incompetence, the diagnosis is almost always missed entirely.

It is evident that the uterine cervix structure determines its elastic nature, and hence its degree of competence. An increased water content changes the tissue density, and hence changes the sound velocity in the cervix. In vitro measurement of the sound velocity has been carried out using the so-called Beam-Tracking technique. A correlation has been derived between the measured velocity and the histological configuration of the cervix.

The aim of this paper is to report the feasibility of using sound velocity to predict cervical changes that could diagnose the structural development of cervical incompetence, regardless of the past history.

Key words: ultrasound velocity, cervix uteri, incompetence, elastin, collagen

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Until the eighth week of pregnancy the structural configuration of the body, isthmus and cervix is the same as in the nonpregnant uterus. Until the twelfth week there is hypertrophy with consequent lengthening and thickening of the isthmus, as takes place in the rest of the uterine body.

The cervix consists mainly of fibrous tissue with varying quantities of smooth muscle; the inner part of the cervix is mainly collagenous, with some scattered nonfunctional muscle fibers.

During labor, elevation of the proportion of mucopolysaccharide to collagen above a critical level is associated with an influx of water into the tissues. This produces an imbalance between the cohesive and dispersive forces interacting between collagen structural units. Immediately postpartum the excess water is absorbed, and the cervical collagen structure returns to its prepartum level of compliance [1].

It is thus clear that the uterine cervix structure determines its elastic nature, and hence its degree of competence. An increased water content changes the tissue elasticity and density, and hence changes the sound velocity of the cervix.

During pregnancy considerable changes take place in the shape and dimensions of the uterus as well as the structure of its muscle. The uterine muscle hypertrophies despite its relative inactivity. This is unusual for a muscular organ, and it is made possible by the pregnancy-maintaining hormonal influence of progesterone.

At the end of pregnancy the uterus consists of 45% muscle and 55% connective tissue. The uterine cervix consists, on the other hand, of only 15% muscle tissue and 85% connective tissue. The muscle fibers of the uterus are integrated into bundles of connective tissue, the compliance of which enables the uterus to adapt to any required volume.

Passive mechanical properties of the uterine muscles in vitro were reported by several investigators. From step-loading of tensile measurements, the following elastic moduli were calculated (at 0.07 MPa stress).

0.6 MPa	pregnant uterus
1 MPa	nonpregnant uterus

which emphasizes that the water content in the pregnant cervix causes imbalance between the depressive and cohesive forces [2].

The cervical tissue consists mainly of closely packed collagenous fibers, arranged circumferentially with only a small amount of muscle (10-15%). Towards the end of pregnancy significant transformation in the structure of the cervical tissue occurs to prepare it for its dilatation during labor.

During pregnancy the cervix consists mainly of fibrous tissue with varying quantities of smooth muscle. The proportion of smooth muscle ranges from 2 to 40%, with an average of 10%.

The histology of 40 uterine cut sections showed that the proportion of smooth muscle cells in the corpus was 28%, in the isthmus 15% and in the cervix 8%. In pregnancy it was found that the amount of muscle in the corpus increased to 42% but that there was a negligible increase in the cervix so that the reduction in muscle from above downwards was even greater than in the non-pregnant uterus [3].

THE ROLE OF SOUND VELOCITY

Measurement of the sound velocity in an elastic tissue will give information about its density and elasticity. This is because the speed of propagation in that kind of tissue is:

$$c = \left[\frac{E}{\rho} \frac{(1-\delta)}{(1+\delta)(1-2\delta)} \right]^{1/2} \quad (1)$$

where E is Young's modulus of elasticity, ρ the density, and δ Poisson's ratio.

Each kind of tissue has its characteristic density and elasticity and hence a characteristic speed c of propagation for longitudinal oscillations. Typical values are:

Fat tissue 1476 m/s
Muscle tissue 1568 m/s
Liver tissue 1570 m/s

Changes in elasticity and/or density of the tissue will accordingly appear as a change in the sound velocity, provided they do not change by a constant ratio [4].

The speed of ultrasound propagation in soft tissue is thought to have a mean value of 1540 m/s. Moreover, the variation in the speed of sound around this mean value is rather small, on the order of ± 5%. Data for pathological tissue are quite rare in the literature, with some noted exceptions. It must be stressed that the overwhelming bulk of the velocity data reported in the literature are derived from excised tissue in vitro, and as such some questions linger as to the strict validity of these data when applied to the in vivo case [5].

METHODOLOGY

Sound velocity estimation has been essentially carried out using the so-called Beam Tracking technique, presented here for convenience. The basic configuration is illustrated in Fig. 1 [6].

Two coplanar transducers are positioned such that their beam axes intersect at right angles. One transducer serves as a transmitter, while the other one as a receiver. A short pulse is first emitted from the transmitting transducer. The energy scattered from the volume of beam intersection V_1 arrives at the receiving transducer located at position R_1 at time t_1 after the emission of the pulse. The receiving transducer is then moved to a new location R_2, separated from the previous location R_1 by a distance dx. The new arrival time of the scattered energy from volume V_2 is now t_2, and let $dt_1 = t_2 - t_1$. The receiving transducer is moved again to location R_3, and the quantity $dt_2 = t_3 - t_2$ is again measured, and so on.

The tracking excursion dx, which is under user control, depends on the characteristics of the transducer radiation field and the scattering properties of the target; a typical value dx = 1mm. After the receiving transducer has been positioned in n locations and (n-1) values of dt have been measured (where typically $10 \leq n \leq 100$), a plot is made of dt vs. dx.

A least square linear regression fit is performed, and the slope of this fit is the estimate of the reciprocal of the speed of sound along the path of the transmitted pulse. Variations in the speed of sound along this path are averaged out by the linear regression process (Fig. 2) [6].

It has been shown that the precision of the estimate of the reciprocal of the speed of sound is given by:

$$\text{precision}(1/\hat{c}) = \pm 2 \left[\frac{3s^2\, dx}{m l^3} \right]^{1/2}$$

where s^2 is the estimated variance of the residuals, l is the total length of the track, and m is the number of uncorrelated tracks [7].

The Beam Tracking Technique has been preferably selected, because it leads to a differential measurement at the section to be investigated, whereas other methods, such as the transmission or substitution method only give an average measurement of different sections. Besides, we have to use a tomographic setup when applying the transmission method.

The two probes of the NE4121 diasonoscope can be used as the transmitting and receiving transducer. That instrument has been primarily designed for echoencephalography, but yet it can be used as an excellent ultrasound source for A-mode screening [8].

Regarding the pulse arriving delays (in the μs range), they have been precisely predicted using the Tektronix 2230, 100 MHz digital storage oscilloscope [9].

EXPERIMENTAL WORK

The Beam Tracking setup that was used is shown in Fig. 3. Two 2.5 MHz, 23mm transducers have been mounted on an X-Y mechanical precision positioning system such that their axes of radiation intersect in a plane at right angles. The path length has been incremented in 1mm steps. After full-wave demodulation and low-pass filtering, the A-mode received signal is shown in Fig. 4. The digital oscilloscope was used to measure the time delays (in the order of 50 μs). The process was repeated 15-20 times, and the measured data were supplied to a program which calculates the precision of the velocity estimate, and performs the linear regression of dx vs. dt.

All cervical uterine samples were subjected to speed of sound measurements, immediately followed by pathological tests, in an attempt to measure the relative amounts of collagen fibers, elastic fibers, as well as smooth muscle in the region of the internal os. Several sections were taken in that region, viewed under light microscopy at 35X magnification, and photographed. Then they were graded for percentage collagen, percentage elastin and percentage smooth muscle. This was mainly the job of the Clinical Pathology Lab at Cairo University. A grading error of 10-15% was expected, owing to parametric inaccuracies.

RESULTS

Fig. 5 shows typical Beam Tracking experimental data. Each of Figs. 6a to 6h depicts a stained section in the cervix following hysterectomy, showing the elastic fiber distribution in the cervical musculature.

Data of the average estimated velocity, the precision factor of the reciprocal velocity estimate (Eq. 2), the percentage collagen, the percentage elastin, and the collagen to smooth muscle ratio, the acoustic impedance, the attenuated fraction, and the mean grey level (Grey level scale = 64) for each of the eight cases, whose sections are depicted in Figs. 6a to 6h, are tabulated in Table 1.

It is of particular interest to point out that the percentage collagen and elastin, as well as the relative amount of smooth muscle have been estimated from planimetric analysis of the stained sections of Figs. 6a to 6h. A software has been also developed by an assistant to the research team that is capable of computing the attenuation constant and the characteristic impedance for a particular region of interest (ROI) of a given texture from the B-mode image, the two parameters having been basically computed from the radiofrequency signal before. Attenuation was briefly computed by extracting the same ROI at the frequencies 4 and 5 MHz, and the grey levels in each row in the region were averaged. The resulting averaged grey levels were exponentially fitted as a function of the depth to obtain the attenuation constant for each of the two frequencies. The overall attenuation constant (in Np/cm/MHz) turns out to be the difference of those two attenuation constants.

The mean grey level (MGL) can also be easily computed from the B-mode image, however the research team has sought to integrate the area under the A-mode signal that corresponds to the cervical region, and divide by the depth of the cervix to obtain the average amplitude.

Fig. 7 shows the velocity distribution vs. percentage collagen and elastin, whereas Fig. 8 shows the velocity distribution vs. collagen to smooth muscle ratio. In Fig. 9 the in vitro sound velocity has been plotted against the MGL. In vivo MGL distribution at different stages of pregnancy for one and the same case is depicted in Fig. 10.

Fig. 11 depicts the velocity distribution during pregnancy for both cases, the competent, as well as the incompetent (with one and the same subject being examined for each condition). The incompetent cervix has continued to sustain pregnancy after undergoing circulage, an operation following which progesterone hormone and sedatives are added. The operation is performed after the 14th week, so that the placenta is formed and there is no possibility of abortion due to congenital anomalies of the embryo. Fig. 12 displays the distribution of velocity and attenuation vs. cervical collagen.

DISCUSSION

It is evident from Eq. 1 that the sound velocity is proportional to the square root of the elastic modulus.

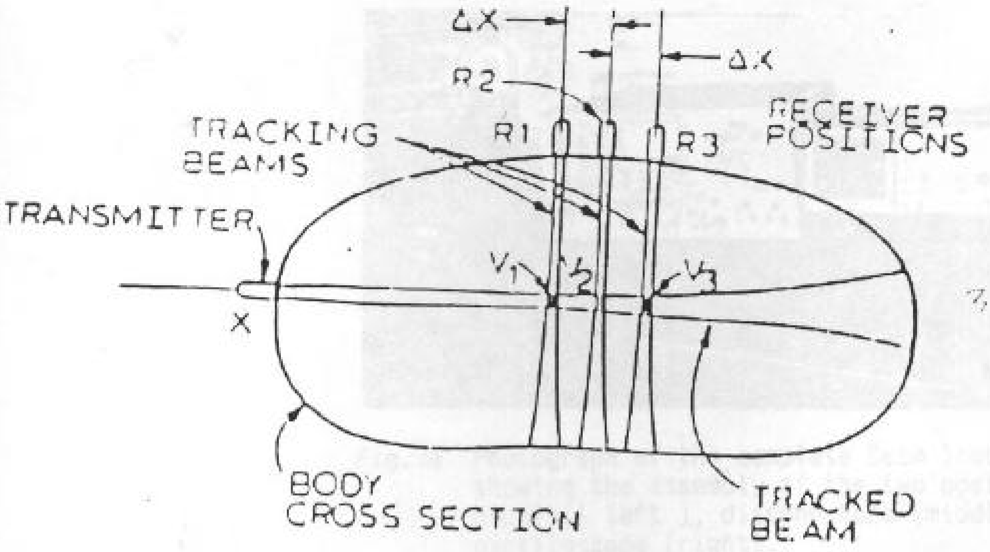
The consistency of the uterine cervix is different in nonpregnant and pregnant women. The non-pregnant cervix usually has a firm consistency, however, the cervix gradually softens as the hygroscopic quality of the cervical connective tissues increases and the binding substance becomes looser. An increased water content changes the tissue elasticity and density and, hence, the sound velocity of the cervix [4]. In the incompetent cervix the binding tissue becomes even looser, and the velocity is markedly reduced late in the first trimester.

As stated before there is no reported structural change whether in the isthmus, body or cervix during the first eight weeks, and since incompetence is completely assessed by the end of the first trimester, we can dramatically predict whether a cervix is competent or not by the anatomical and histological changes the cervix undergoes during the eighth to twelfth week.

Because of the elevated water content, as pregnancy progresses, the cervix becomes considerably hypoechogenic, and consequently the mean grey level for a selected ROI on a conventional B-scan is depressed. In our new approach, the mean grey level has also been correlated to the velocity.

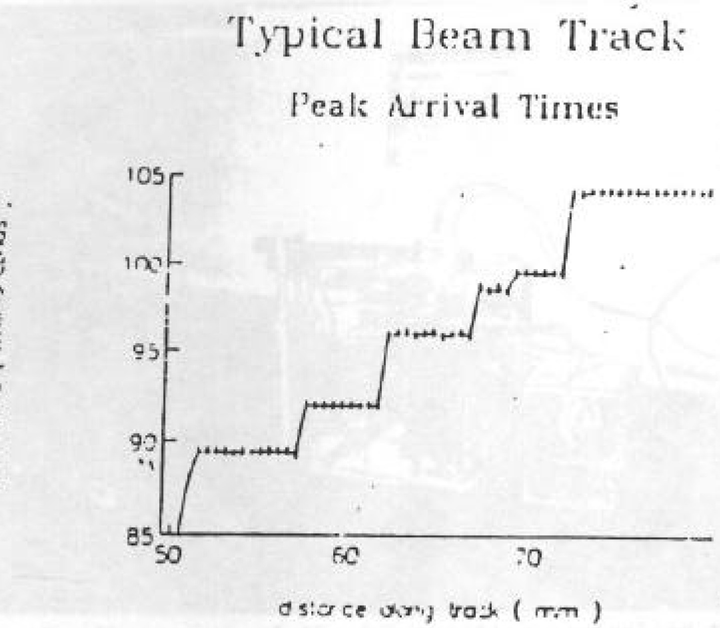
TABLE 1

CASE #	Fig.	Average Estimated Velocity (m/s)	Precision	Collagen	Elastin	Collagen/Smooth Muscle	Impedance (kg/m^2sec)	Attenuated Fraction	MGL
1	6a	1570.0	±0.9%	21%	50%	0.75	1579.5	0.107	27.5
2	6b	1601.7	±3.1%	25%	47%	0.96	not measured	0.112	28.4
3	6c	1618.0	±3.7%	28%	42%	1.10	not measured	0.116	28.8
4	6d	1625.8	±1.9%	33%	35%	1.25	not measured	0.118	29.0
5	6e	1628.2	±2.0%	30%	40%	1.30	1720.0	0.122	29.1
6	6f	1629.7	±3.1%	47%	25%	1.96	1664.7	0.135	30.8
7	6g	1636.5	±3.1%	50%	20%	2.16	1733.0	0.139	31.0
8	6h	1670.3	±2.2%	67%	13%	4.80	1789.8	0.151	31.3



Basic Beam Tracking concept.

Fig. 1



Typical experimental stairstep data obtained by tracking over 30mm and recording the arrival time of the peak of the echo complex.

Fig. 2

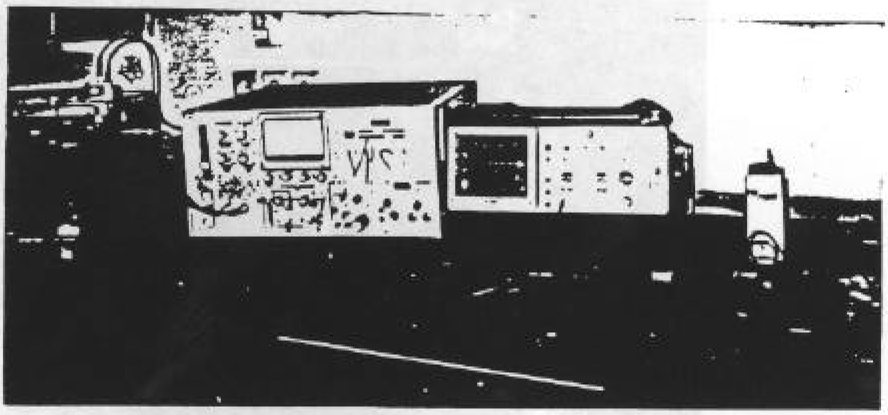


Fig.3a Photograph of the complete Beam Tracking experimental setup, showing the assembly of the two position-controlled transducers (left), diasonoscope (middle), and digital storage oscilloscope (right).

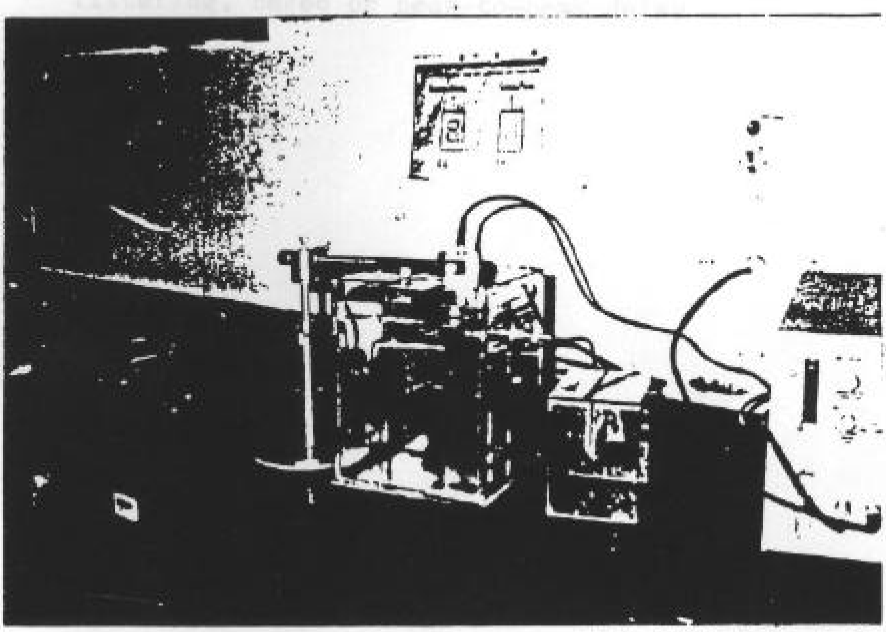


Fig.3b. Photograph of the two position-controlled transducers placed in an aquarium, and connected to the diasonoscope (partly shown in figure).

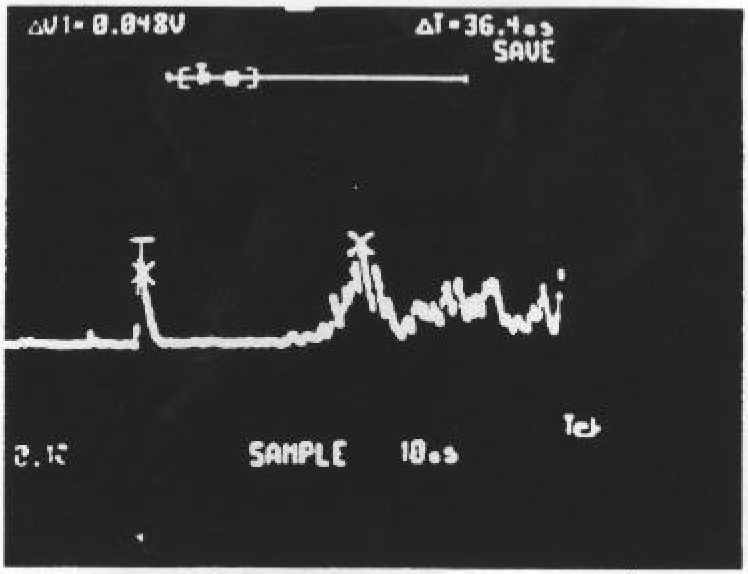


Fig. 4. Typical demodulated signal, sampled at 2.5 MHz and 12 bits with 100-kHz lowpass filtering, based on peak-to-peak delay measurement

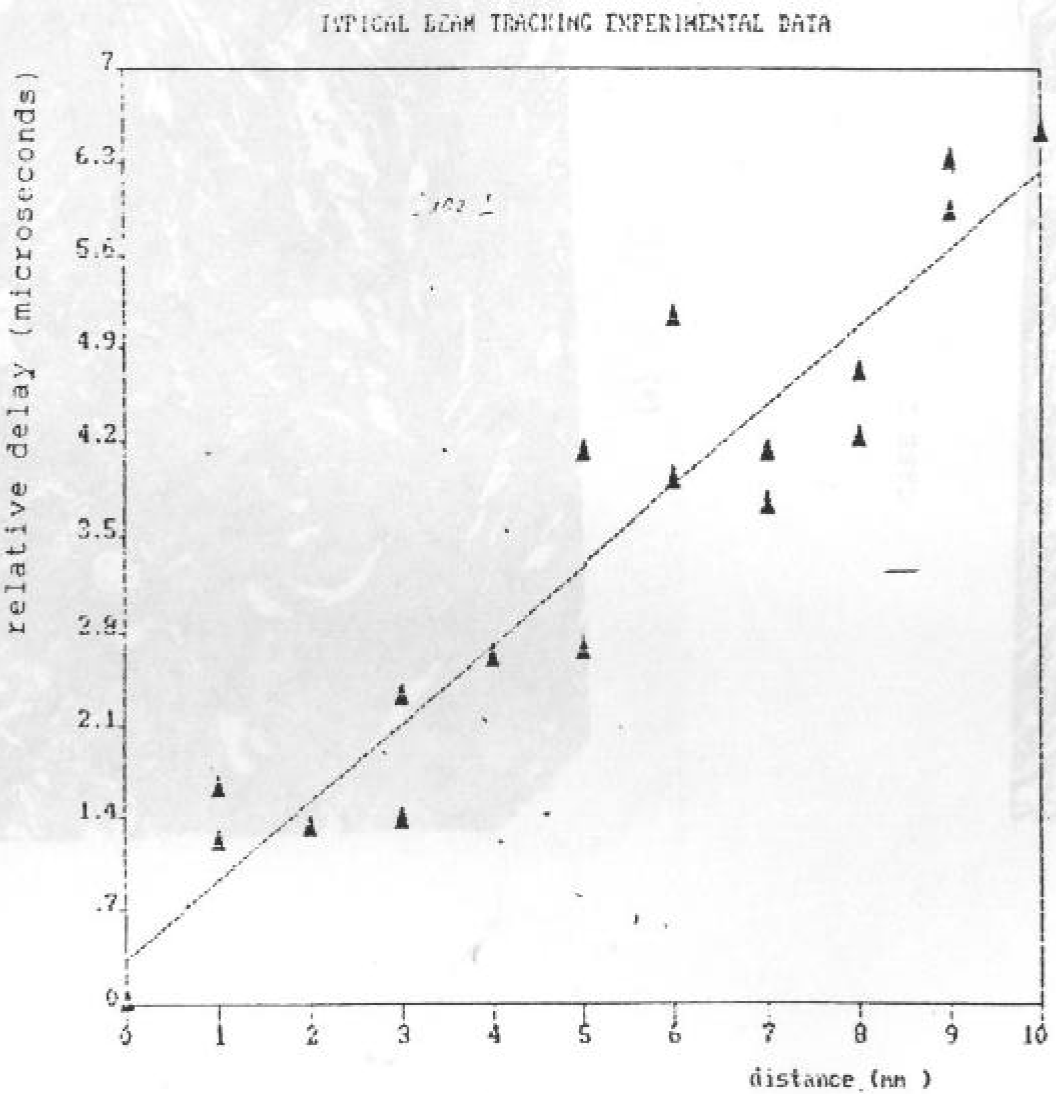

TYPICAL BEAM TRACKING EXPERIMENTAL DATA
relative delay (microseconds)
7
6.3
5.6
4.9
4.2
3.5
2.8
2.1
1.4
.7
0
0
1
2
3
4
5
6
7
8
9
10
distance (mm)

Fig. 5

CASE 1

(a)

CASE 2

(b)

Fig.6

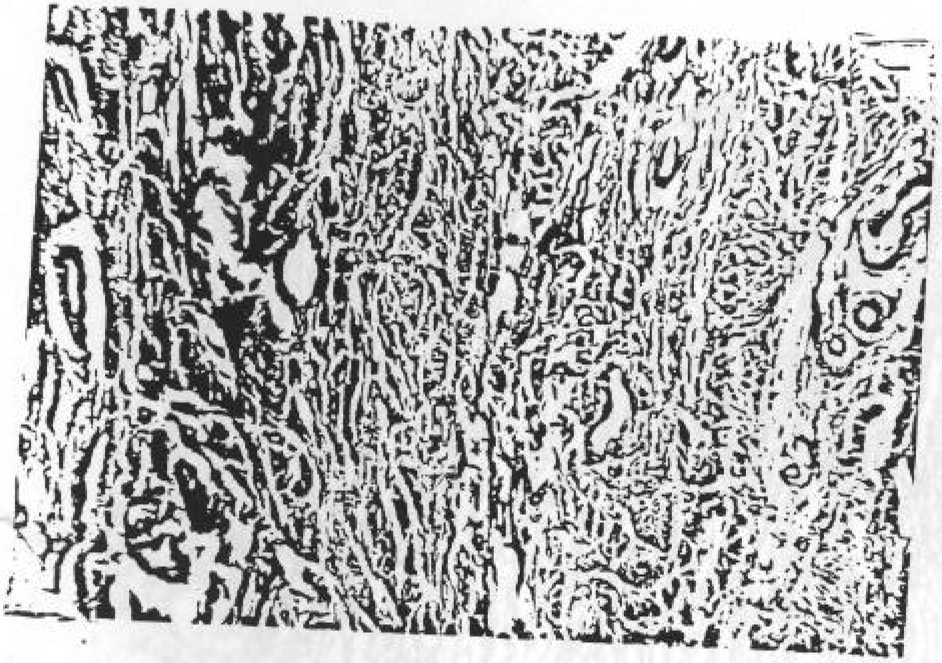
CASE 3

(c)

CASE 4

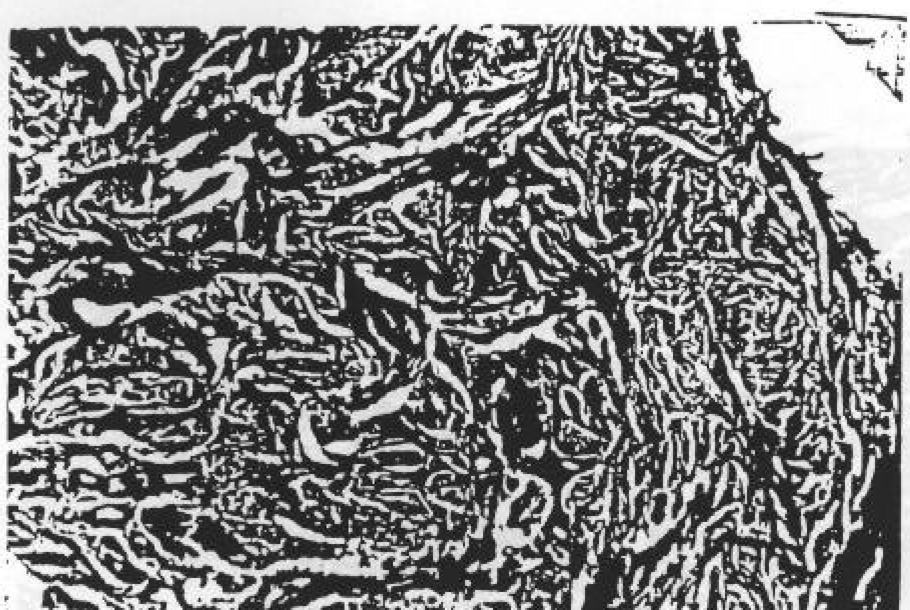
(d)

CASE 5



(e)

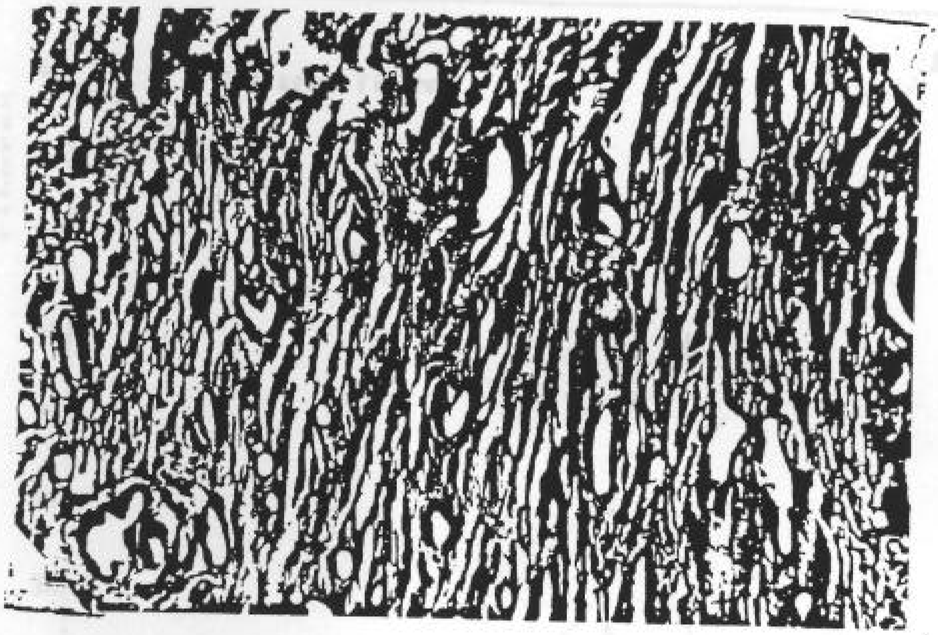
CASE 6



(f)

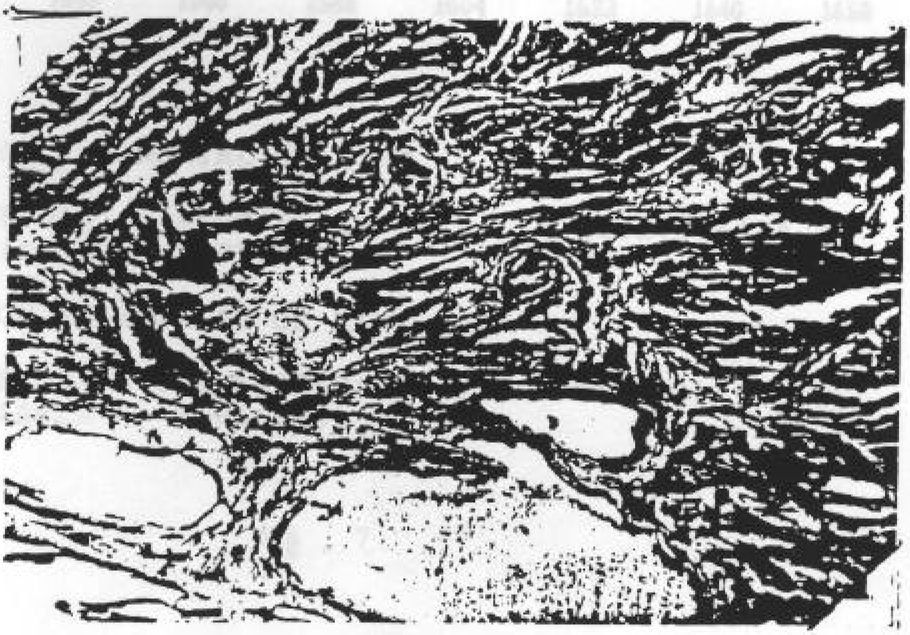
Fig.6

CASE 7



(g)

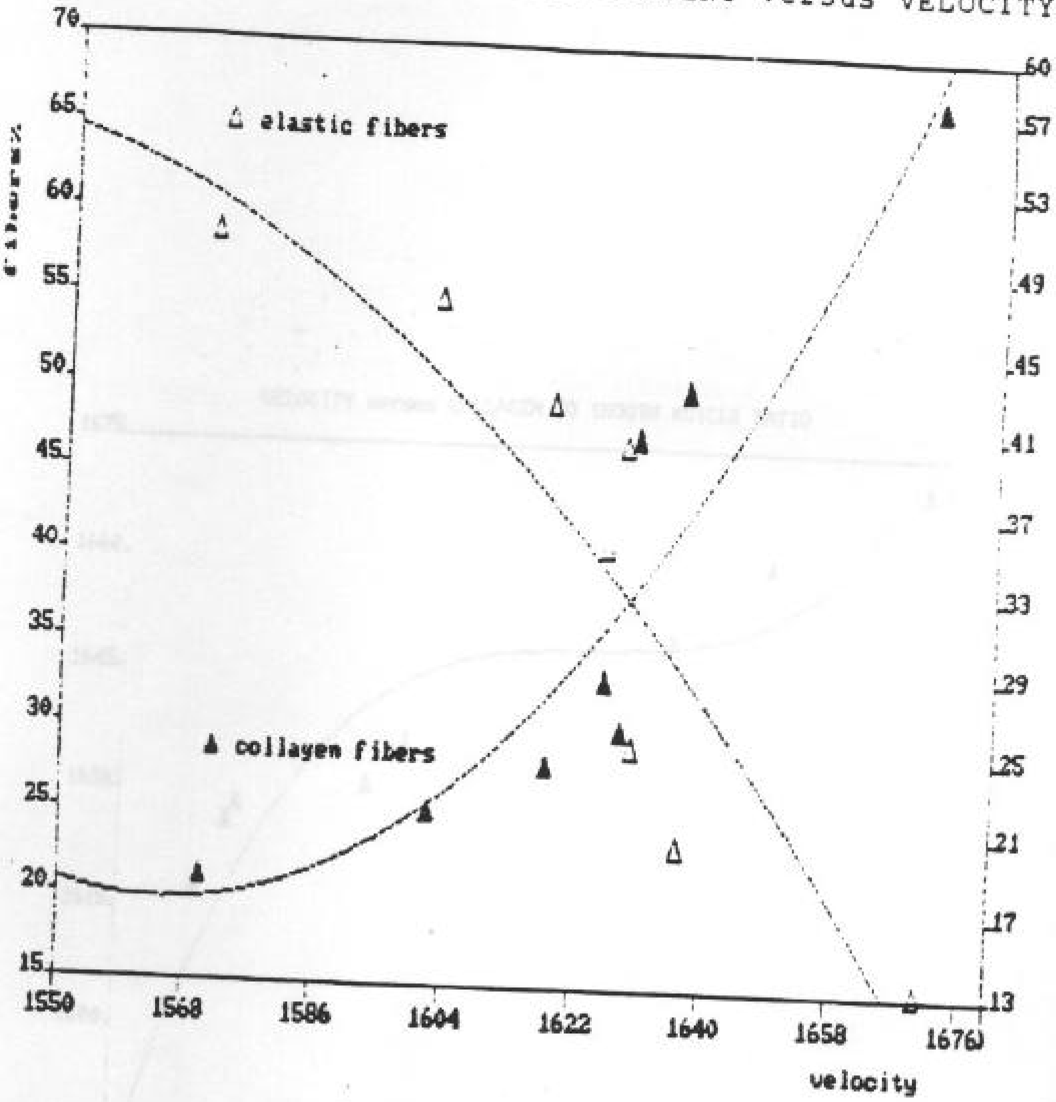
CASE 8



(h)

Fig.6

ELASTIC and COLLAGEN FIBER CONTENT versus VELOCITY



THE REGRESSION POLYNOMIAL OF LINE 1 -

(2.078E+01) + (-1.741E+01)*X + (7.501E+01)*X^ 2
THE VARIANCE - 2.771E+01

THE REGRESSION POLYNOMIAL OF LINE 2 -

(5.528E+01) + (-1.552E+01)*X + (-3.566E+01)*X^ 2
THE VARIANCE - 2.901E+01

Fig . 7

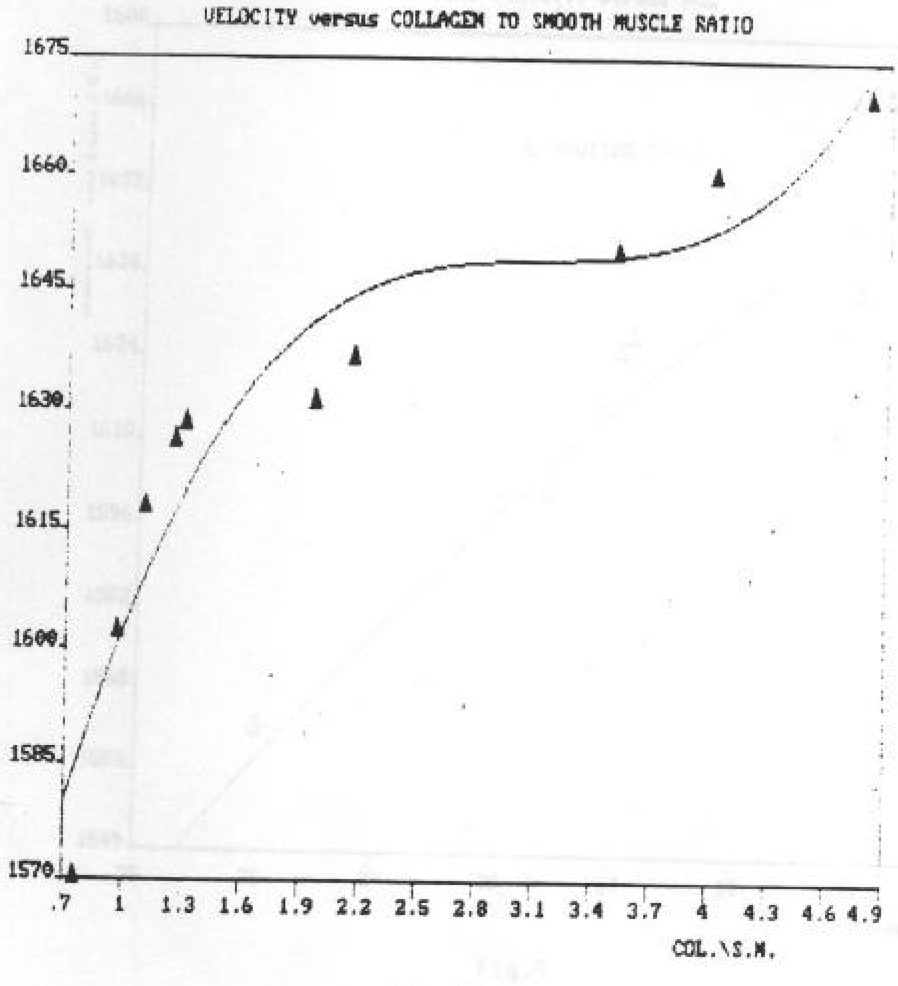

VELOCITY versus COLLAGEN TO SMOOTH MUSCLE RATIO
1675
1660
1645
1630
1615
1600
1585
1570
.7 1 1.3 1.6 1.9 2.2 2.5 2.8 3.1 3.4 3.7 4 4.3 4.6 4.9
COL.\S.M.

Fig. 8

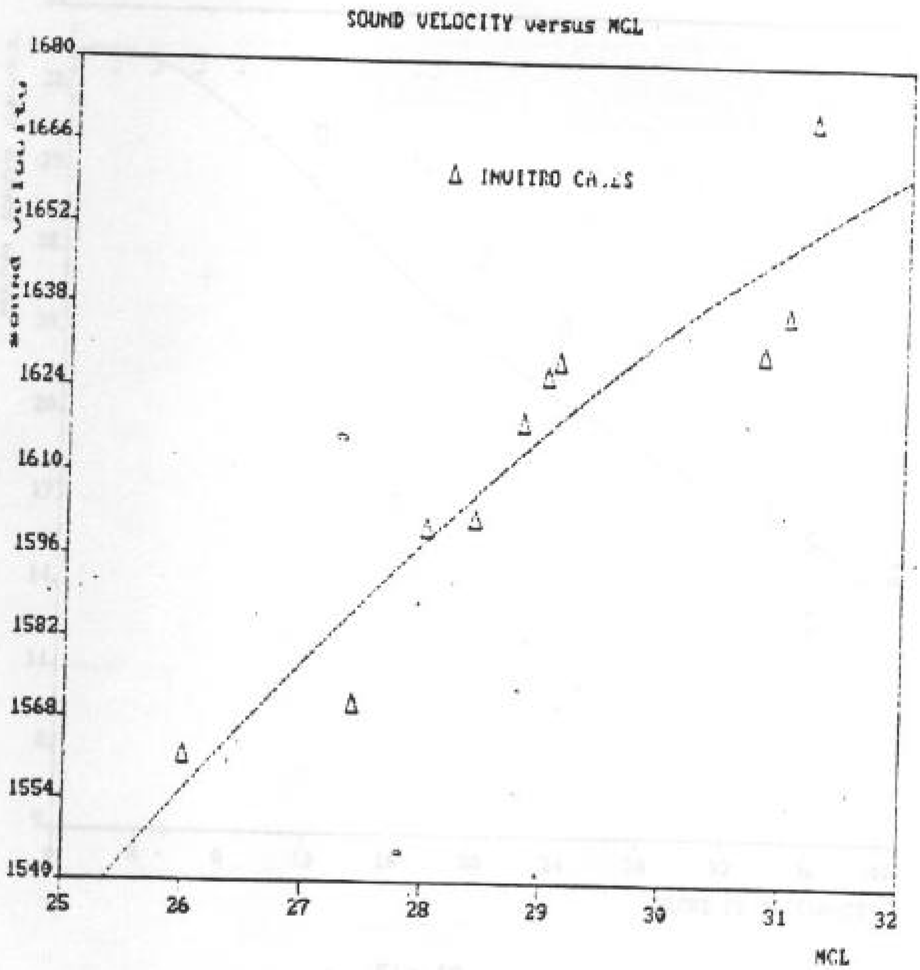

SOUND VELOCITY versus MCL
Sound velocity
1680
1666
1652
1638
1624
1610
1596
1582
1568
1554
1549
Δ INVITRO CASES
25
26
27
28
29
30
31
32
MCL

Fig.9

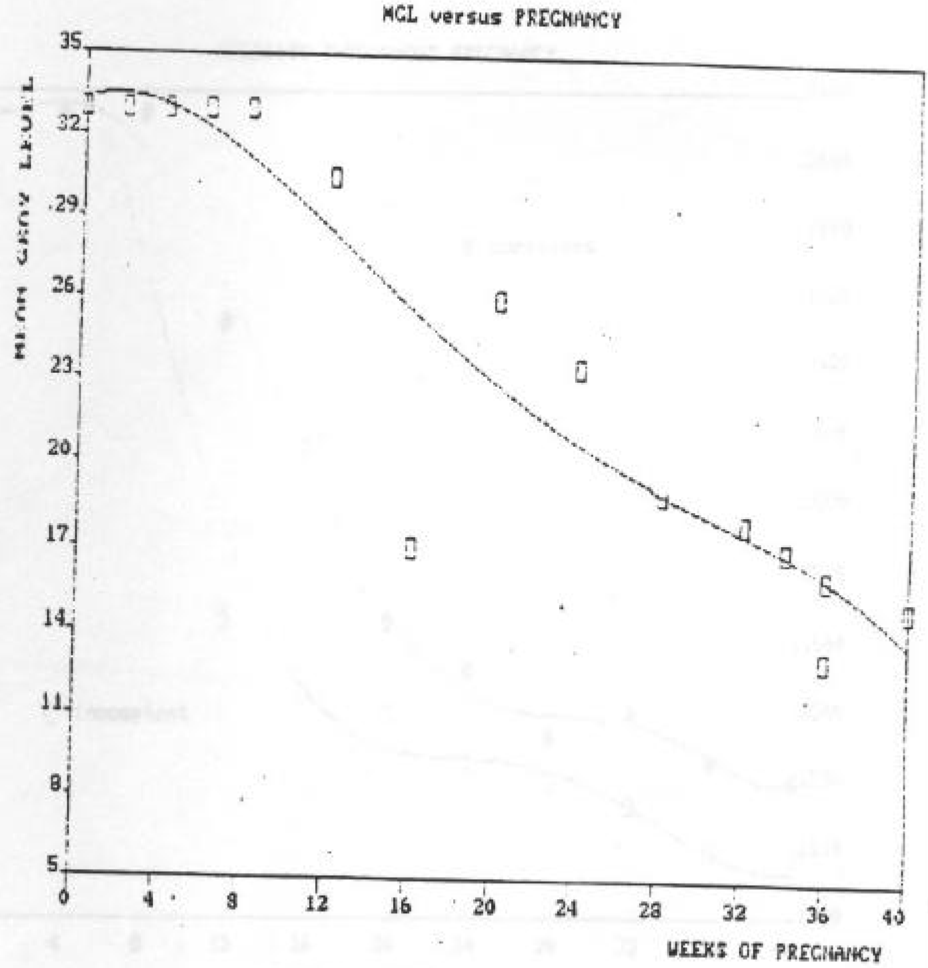

MCL versus PREGNANCY
35
32
29
26
23
20
17
14
11
8
5
0
4
8
12
16
20
24
28
32
36
40
WEEKS OF PREGNANCY

Fig.10

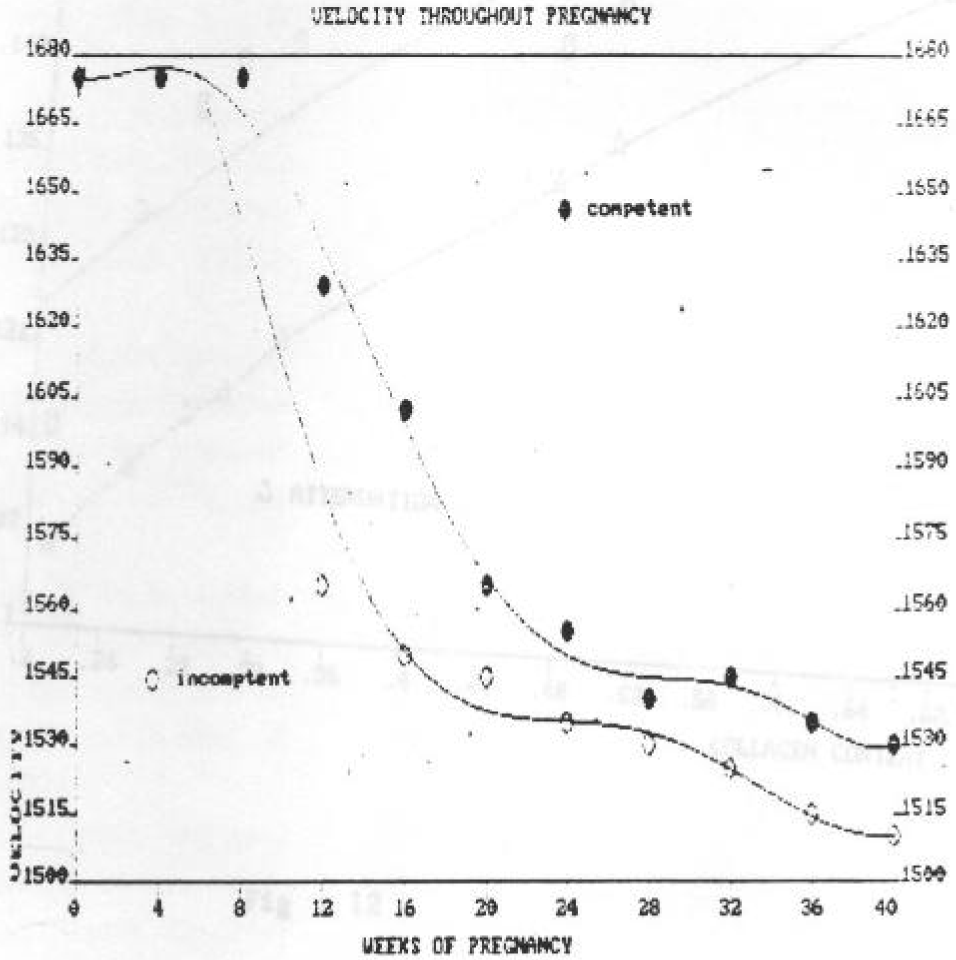
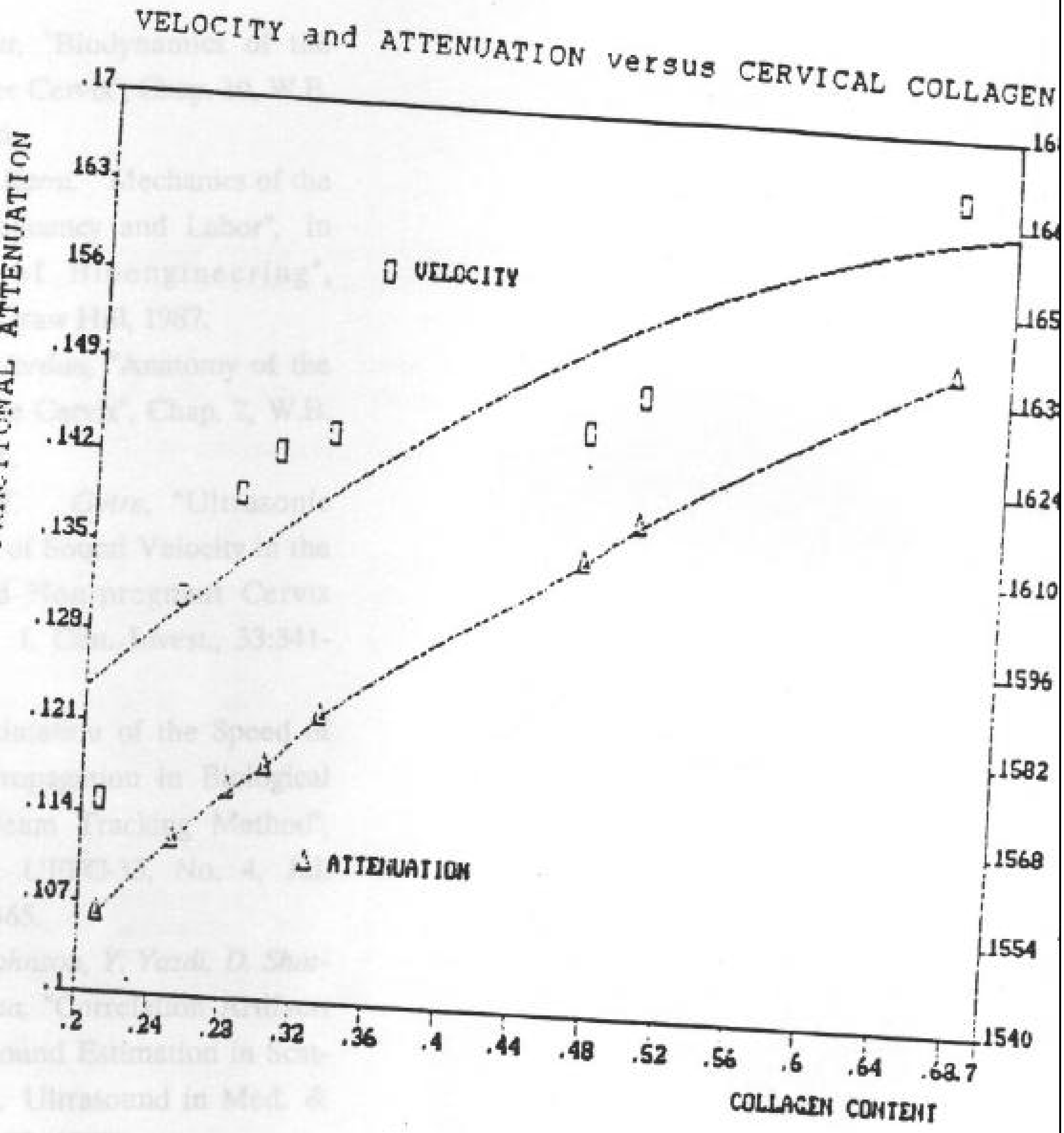

VELOCITY THROUGHOUT PREGNANCY
competent
incomptent
VELOCITY
WEEKS OF PREGNANCY
1680
1665
1650
1635
1620
1605
1590
1575
1560
1545
1530
1515
1500
0
4
8
12
16
20
24
28
32
36
40

Fig.11



VELOCITY and ATTENUATION versus CERVICAL COLLAGEN
FRACTIONAL ATTENUATION
VELOCITY
ATTENUATION
COLLAGEN CONTENT
.17
.163
.156
.149
.142
.135
.128
.121
.114
.107
.1
.2
.24
.28
.32
.36
.4
.44
.48
.52
.56
.6
.64
.68.7
1596
1582
1568
1554
1540

Fig . 12

REFERENCES

1] *R.H. Phillpott,* "Biodynamics of the Cervix", in "The Cervix", Chap. 10, W.B. Saunders, 1976.

2] *J. Mizrahi, Z. Karni,* "Mechanics of the Uterus in Pregnancy and Labor", in "Handbook of Bioengineering", Chap.10, Mc. Graw Hill, 1987.

3] *A. Singer, J. Jordan,* "Anatomy of the Cervix", in "The Cervix", Chap. 2, W.B. Saunders, 1976.

4] *T. Bakke, T. Gytre,* "Ultrasonic Measurement of Sound Velocity in the Pregnant and Non-pregnant Cervix Uteri", Scnad. J. Clin. Invest., 33:341-346 (1974).

5] *J. Ophir,* "Estimation of the Speed of Ultrasound Propagation in Biological Tissues: A Beam Tracking Method", IEEE. Trans. UFFC-33, No. 4, Jul. 1986, pp.359-365.

6] *J. Ophir, W. Johnson, Y. Yazdi, D. Shattuck, D. Mehta,* "Correlation Artifacts in Speed of Sound Estimation in Scattering Media", Ultrasound in Med. & Biol., 15:341-352 (1989).

7] *T. Kontonassios, J. Ophir,* "Variance Reduction of Speed of Sound in Tissues Using the Beam Tracking Method", IEEE Trans. UFFC 34:524-530 (1978).

8] NE4121, Diasonoscope, Operator's Manual, Nucl. Enterprises, Sighthill, Edinburgh, Scotland, Apr. 1976.

9] Using the 2230 Digital Storage Oscilloscope, Tektronix, Oct. 1986.