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Liquid Crystal Microcapsule Medical Device Used for Thermographic Examination of the Human Female Breast

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ABSTRACT

A new medical device called Thermascan has been developed based on heat-sensitive microencapsulated liquid crystals. This thermographic device assists in early detection of breast abnormalities that are characterized by minor changes in tissue temperature and displayed by the color changes in the device. This liquid crystal device is used to screen patients who fall into the average to high risk category. The value of this diagnostic device is that it will detect minute temperature changes that occur in the breast from very small heat-producing cancers.

Index Entries: Key phrases: liquid crystals, microcapsules, microencapsulation, thermography, breast cancer.

INTRODUCTION

According to the American Cancer Society 1982 (*1*), the breast is the most common site of cancers in women. It accounts for over 26% of all the cancers in American women. An estimated 112,000 new cases occurred in the US during 1982. About one out of eleven women will develop breast cancer at some time during her life. An estimated 37,300 deaths occurred in 1982.

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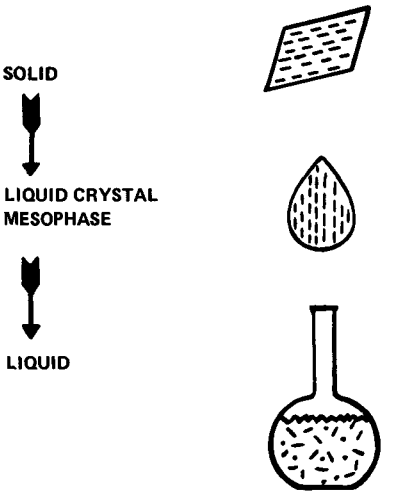


Fig. 1. Phase transition.

THEORETICAL BACKGROUND

Many organic compounds, in the transformation from the solid to the liquid state, pass through an intermediate phase that exhibits the anisotropic or ordered properties of crystalline solids. The term, "Liquid Crystal State" has been coined to describe this mesophase (*see* Fig. 1). The normal phase transition occurring with these materials follows the general path:

Anisotropic crystalline solid → Anisotropic liquid crystal state → Isotropic liquid

The liquid crystal states have been scientifically classified into distinct categories, thermotropic or lyotropic, based on the mode of penetration into the liquid crystalline region, the type of ordering, and the degree of spatial arrangement of the molecules in the mass of the material. In the thermotropic-type liquid crystals, this phase transition is induced by temperature change. Thermotropic liquid crystals, more specifically, the twisted nematic or cholesteric materials, are the compounds that are amenable to microencapsulation and device construction.

Molecules that traverse the cholesteric liquid crystalline state are normally long and rod-shaped. They are oriented in planar configurations in the mass of the material. The cholesteric or twisted nematic structure is depicted in Fig. 2. As the temperature changes, the cholesteric structure twists and tilts. As a result of the unique structure of this mesophase, iridescent refracted colors are observed in the materials when they are illuminated with white light.

A cholesteric liquid crystal system, when formulated properly, responds to changes in temperature by sequentially reflecting the complete

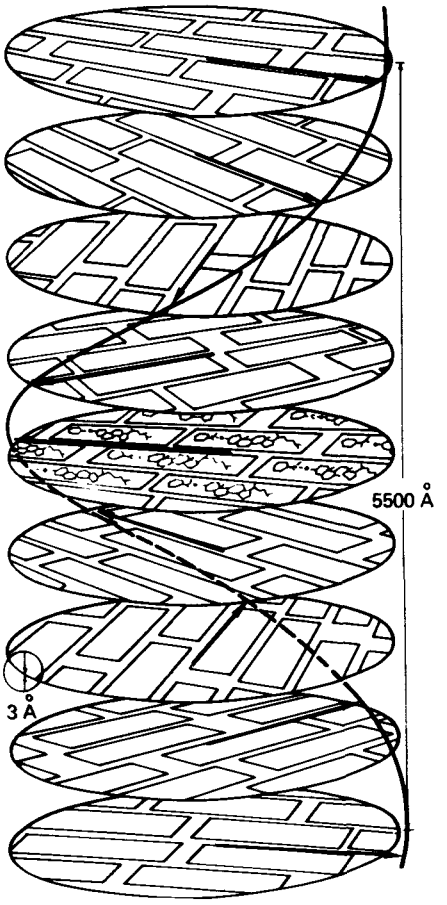


Fig. 2. Cholesteric liquid crystal structure.

visible spectrum from red to violet. Colors reflected by liquid crystals represent only a fraction of the incident light. The remaining portion of the incident light is transmitted and scattered by the liquid crystals. Consequently, the liquid crystals are normally used in combination with an absorptive black background. This black background absorbs the scattered light and thus intensifies the reflected colors. The black background is also used with microencapsulated liquid crystals.

Table 1 lists representative cholesteric esters that can be formulated. By varying the ratios of two or more of the materials, various thermal responses are obtained. Material variations not only change the initial event temperature defined as start of red, but also enable one to vary the color band widths; namely, start of red to start of blue as a function of temperature.

Liquid crystals are formulated to obtain a specific event temperature and display over a predetermined colorplay range. To accomplish this, the ratio of three specific liquid crystal raw materials can be varied to ob-

TABLE 1
Representative Liquid Crystal Material

Cholesteryl chloride
Cholesteryl isostearylcarbonate
Cholesteryl myristate
Cholesteryl oleylcarbonate
Cholesteryl pelargonate
Cholesteryl propionate

tain the desired event temperatures and colorplay ranges. In the phase diagram presented in Fig. 3, the concentration of component A and B can be changed to obtain the starting event temperature. Component C, which has been held at a constant concentration, controls the colorplay range—start of red to start of blue. By varying the concentration of component C, the colorplay range can be altered. Increasing the concentration of component C also depresses the starting event temperature. Thus, by changing the liquid crystal components and their concentrations, a variety of temperature-responsive liquid crystal formulations can be produced and subsequently microencapsulated.

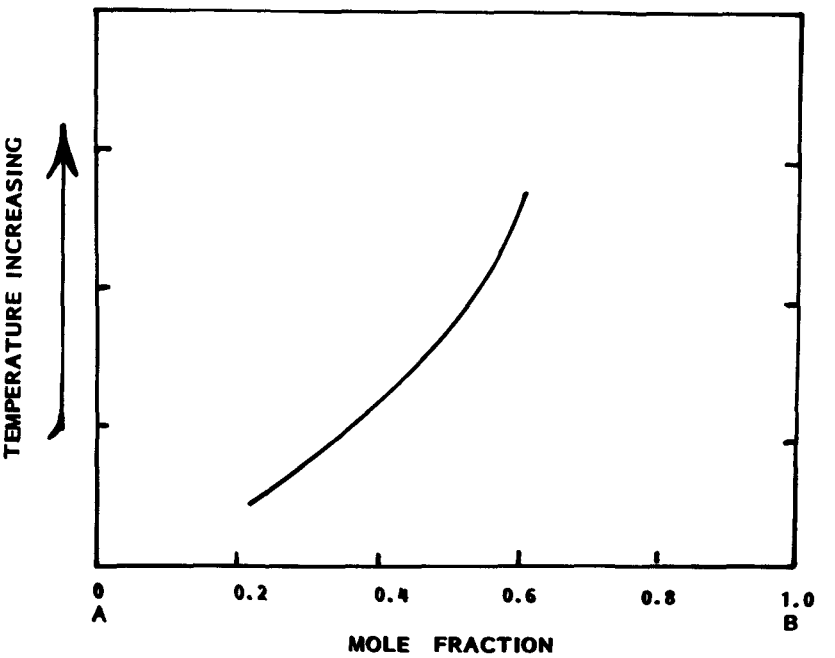


Fig. 3. Liquid crystal formulations (3 components: A & B variable, C constant).

Microencapsulated liquid crystal systems offer several major advantages over unencapsulated forms of these materials. Some of these advantages are listed below: Microencapsulation

- Prevents contamination of the labile material
- Enhances stability
- Reduces angular dependence of the formulations
- Permits simultaneous use of more than one temperature range
- Provides for permanent geometrical designs

The microencapsulation of liquid crystals is accomplished by a classical coacervation process. The process is a batch type, consisting of a series of three steps carried out under continuous and variable speed agitation. The three process steps are schematically illustrated in Fig. 4. Step one of the process is the formation of three immiscible chemical phases: an aqueous liquid-manufacturing vehicle phase, a core material phase

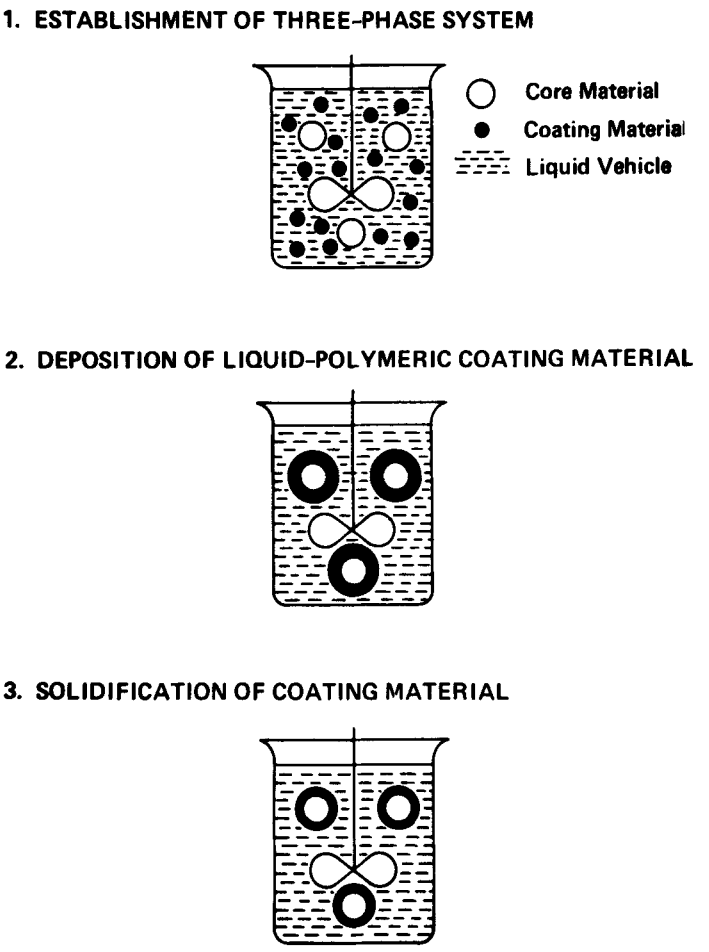


Fig. 4. Microencapsulation process schematic.

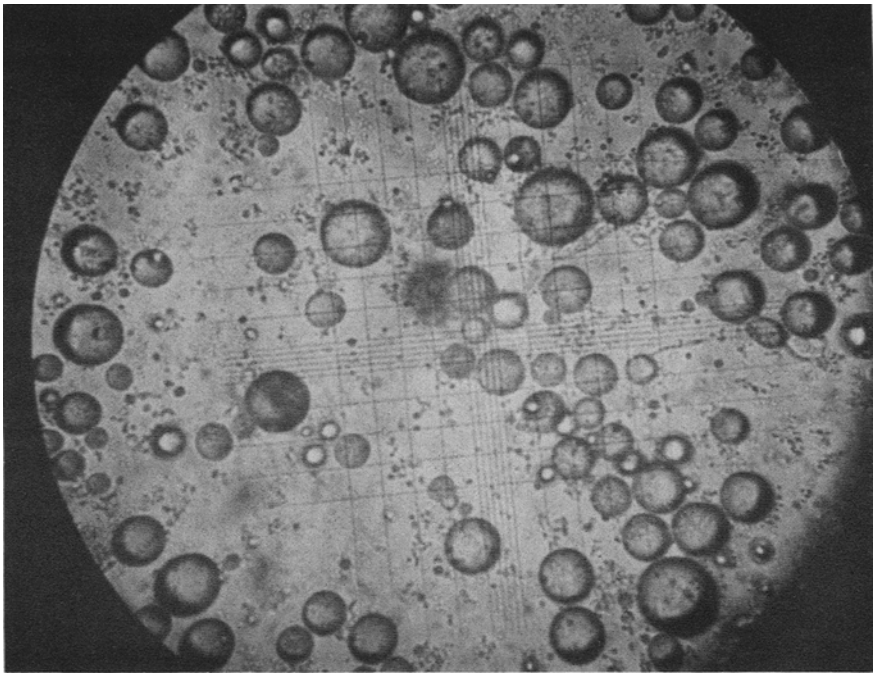


Fig. 5. Photomicrographic of liquid crystal microcapsules.

(namely, a liquid crystal formulation), and a liquid coating material phase (the coacervate) comprised of a hydrocolloid complex. Step two of the process consists of depositing the liquid polymer coating upon the liquid crystal core material. This is accomplished by controlled, physical mixing of the liquidous coating material and the liquid crystalline material in the water phase while the temperature is lowered at a specific pH. Step three of the process involves solidifying the coating. This is accomplished by cooling the batch and crosslinking the coating to form a self-sustaining microcapsule.

Figure 5 shows liquid crystal microcapsules. The size is well below 100 nm. This microcapsule system has been approved by the FDA for microencapsulating selective food additives.

PROCEDURES

To produce a device that will cover the range of temperatures required in breast thermography, a mixture of two formulations is required. The thermographic color display is exhibited in a temperature band starting at 30°C and continuous through 36°C. The two formulations that are admixed to produce this display each have a 3°C colorplay span; the lower formulation is designed to be active from 30 to 33°C and the second higher formulation from 33 to 36°C. When these formulations are mixed together and applied to a substrate, a dual reinforced color ef-

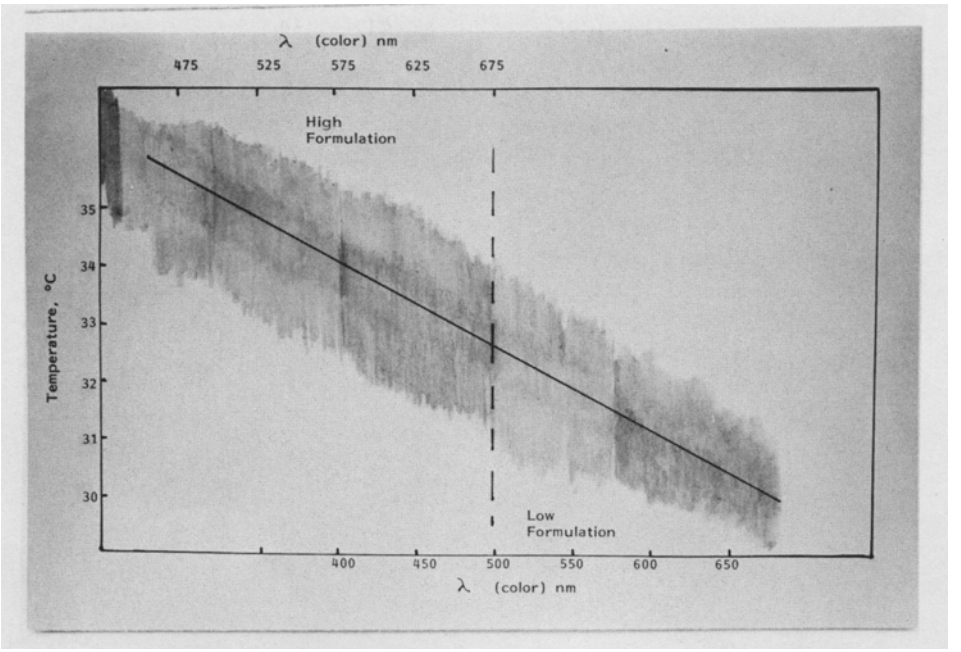


Fig. 6. Thermascan color display.

fect occurs. In other words, there is an overlap of the red and yellow segment of the higher formulation with the blue segment of the lower formulation. This results in a midrange pastel purple effect. This can be seen in the graphical representation presented in Fig. 6.

THE THERMASCAN DEVICE

Figure 7 illustrates the actual structure of the Thermascan device. A transparent film is used as the device substrate. Onto this film are printed windows. The dual formulation microcapsules are applied in the window area. To reinforce the colorplay obtained with microencapsulated liquid crystals, a black absorptive background is applied. Finally, a thin film laminate is placed on the back to protect the device.

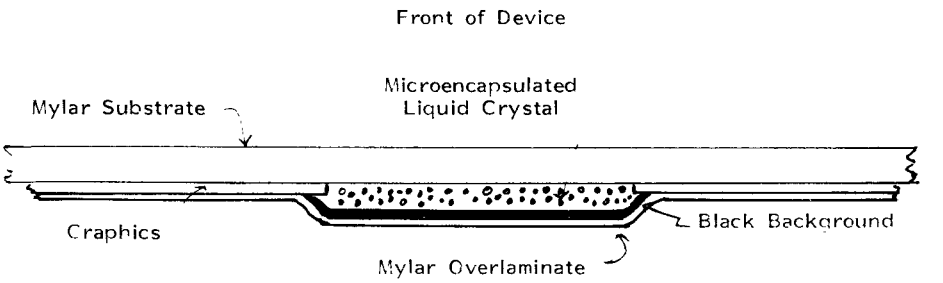


Fig. 7. Structure of Thermascan device.

This overlaminate provides a surface that can be cleaned. The device can be reused many times.

The stability of the event temperatures of the device has been measured when stored in the original package. As can be readily seen from the data in Table 2, the event temperatures have a tendency to increase slightly with time, but in essence are reasonably stable over a period in excess of 1 yr. Because of the fact that the device is used to measure temperature differentials across the surface of skin tissue, the absolute temperatures become less significant.

Figure 8 depicts the device in actual use. The patient disrobes above the waist and equilibrates the upper body against ambient conditions for 5–10 min. The device is then placed across the breasts. Good contact between the back side of the film and the tissue to be measured is important. She then looks into a mirror to observe the image. At this time the patient compares the image in the mirror to a reference colored photograph taken in a physician's office.

A typical normal thermogram is presented in Fig. 9. Very pastel colors including light shades of purple are present. Deep blues are absent from the thermogram.

In Fig. 10 one can see the pastel purples that indicate the start of the second higher event temperature range. In addition, the deep purples associated with high temperatures and a potential problem are present. When this hyperthermic condition exists, the patient should see a physician for further testing to determine the source or reasons for the abnormal thermogram.

In addition to the hot spots exhibited in the previous thermogram, dissimilarity in the pattern from right to left is also indicative of a potential problem. This phenomenon is seen in Fig. 11. If a patient has such an asymmetrical thermogram, she should contact her doctor for further testing to determine whether a problem exists.

The device was proved to be effective in detecting not only cancers of a breast, but also fibrocystic disease and fibroadenomas. In a recent

TABLE 2
Stability of Event Temperature

Number	Test, d	1st Red	1st Blue	2nd Red	2nd Blue
0681	0	27.3	31.2	32.0	33.8
	174	26.9	30.8	32.7	34.6
	450	26.3	31.0	32.2	34.3
817/818	0	30.2	33.4	33.4	36.8
	94	30.6	34.0	33.8	37.2
	192	30.9	34.2	34.1	37.5
823/824	0	29.9	32.9	32.7	36.0
	94	30.1	33.5	33.0	36.4
	192	30.3	33.8	33.3	36.6

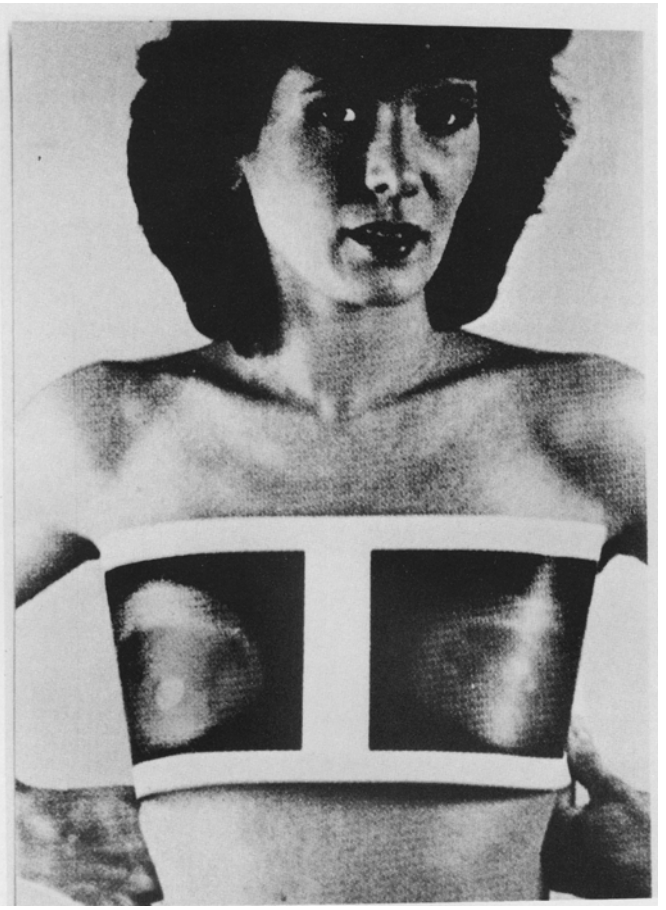
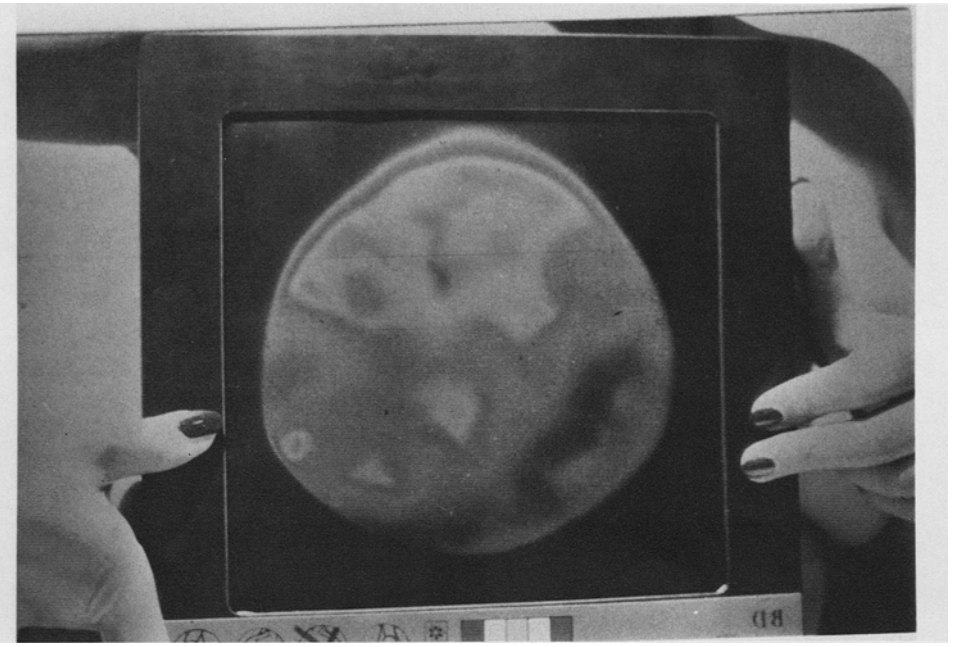


Fig. 8. Thermascan usage (courtesy of BCD Products, Inc.).

study conducted by Ciabre and colleagues (2), Thermascan detected 67 of 72, or 93% of biopsy-confirmed cancers. Thermascan results were classified as suspect on the basis of two fundamental criteria: thermic asymmetry and hyperthermia. Additional good results were found using Thermascan by Orefiled. The method accurately detected twelve of thirteen, or 92% of the cancers. More importantly, four of these patients had Stage One disease or tumor sizes smaller than 2 cm. All lesions were detected by Thermascan. The device even detected a small 0.6 cm lesion. The results were further substantiated in a large West German study of over 900 patients by Von Fournier and coworkers (4). Out of 20 Stage One cancers, at least 80% were detected by Thermascan. In these trials Thermascan compared favorably with other infrared and contact thermographic systems. In addition, the results were found to be in agreement with the results of physical examinations and mammography. The device often detected abnormalities not discovered by these other means.



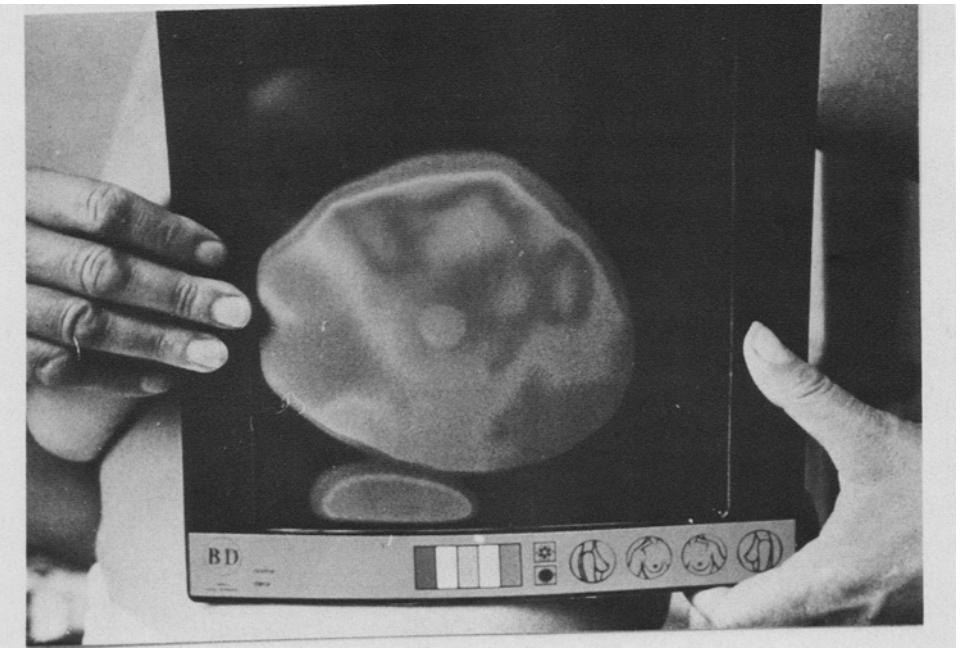


Fig. 10. Abnormal thermogram.

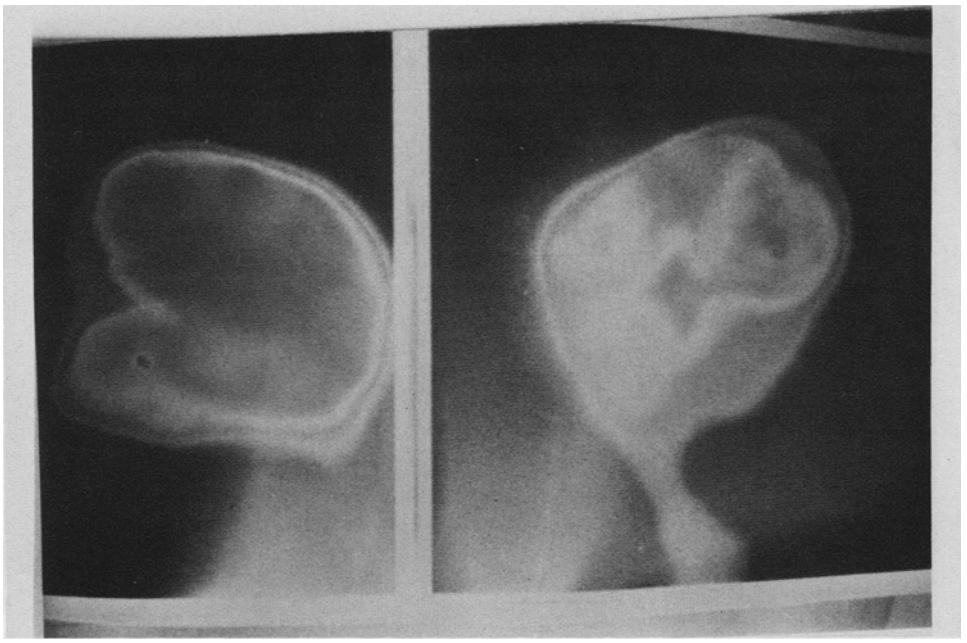


Fig. 11. Abnormal thermogram.

In summary, the thermographic device, employing microencapsulated liquid crystals, can be used to the benefit of humankind. Further experience is needed with this new device to more fully determine its long-range potential. Some of its advantages include its special suitability for continual self-monitoring. It is non-invasive, non-irritating, and a nonradiation method of thermography. It can be reused by the patient many times and is compact and portable. It can be used in the home and the results are easy to interpret.

ACKNOWLEDGMENT

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