TUMOR DETECTION USING MICROWAVE ENHANCED THERMOGRAPHY AND COMPUTER AIDED IMAGE ANALYSIS*

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Abstract

Thermography is an alternative to X-Ray mammography for tumor detection. Sensitivity of thermography is increased by application of low level microwave energy. Data obtained using guinea pig and rat implantable tumors is presented. Computer aided analysis techniques of the data is discussed.

Introduction

Thermography is a viable technique for noninvasive early detection of tumors and is presently being used in conjuction with X-ray mammography and physical examination to detect breast cancer. The use of thermography has recently received greater impetus because of data which imply that the integrated effect of utilizing ionizing radiation on a regular basis for early detection (X-ray mammography) increases the risk of inducing cancer beyond the potential benefits derived from early detection. The universal usage of thermography has, however, been hindered due to the ambiguities associated with thermographic data analysis. These ambiguities result from small skin surface temperature pertubation associated with a small tumor. It is, therefore, difficult to attribute observed small spatial increases in skin surface temperature to the presence of a tumor with the degree of certainty necessary to justify treatment or surgical exploration. Confidence in the thermographic data can be inproved by increasing the spatial temperature gradients.

Experimental Procedures

Experiments have been conducted which have demonstrated that thermographic detectability of tumors can be enhanced by microwave heating. This experimental effort is described by presenting the experimental objectives, the experimental arrangement, and the data acquisition procedure.

Experimental Objective. The primary objective of the experiment performed is to determine if an increase in tumor thermographic detectability can be obtained by irradiating the tumor area with electromagnetic energy. Implicit in this objective is the desire to determine whether or not selective absorption of microwaves in situ is capable of producing a significant increase in observable surface temperature gradients. The demonstration of this effect in the particular instance cited is considered as a necessary step before more extensive tests are proposed.

Experimental Arrangement. The experiment was performed by selectively heating tumors which have been transplanted into guinea pigs and rats. The heating was obtained by irradiating the tumor area with microwave energy. The resulting surface temperature increases were observed using a thermovision camera. The experimental arrangement utilized to accomplish the stated objectives is described below.

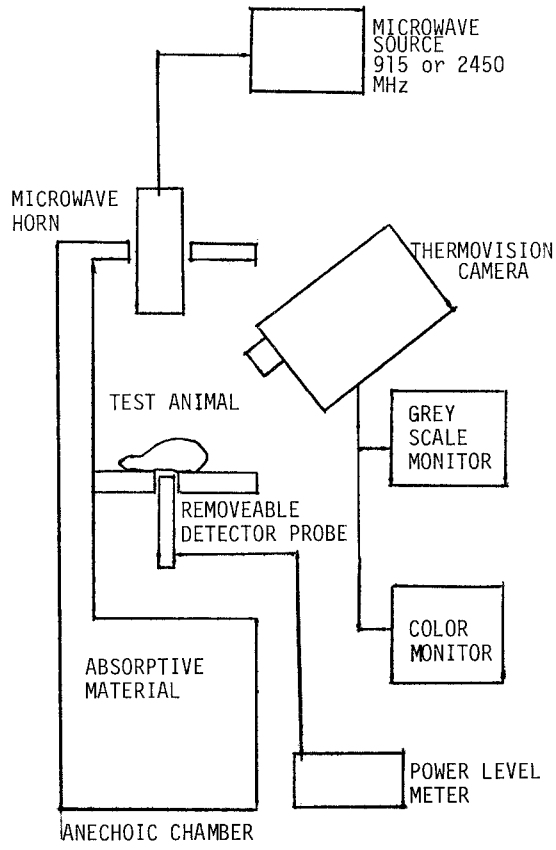


Figure 1. Experimental arrangement for microwave heating of test animal for enhanced thermographic tumor visualization.

A schematic drawing of the experimental arrangement used for the microwave irradiation is shown in Fig. 1. The experimental arrangement consists of a source, a test animal, and a thermovision camera system. Microwave energy was obtained from 2.45-GHz, 400W and 915 MHz, 600W commercial sources. Energy was coupled from the source to the guinea pig using an appropriate waveguide and horn radiator (a horn radiator was used instead of a direct contact applicator to permit simultaneous excitation and thermographic viewing). The effective radiated power density was measured to be 24 mW/cm^2 for the guinea pig data and 100 mW/cm^2 for the rat data. Spatial measurements indicate that this power density is uniform within 4% over an area exceeding $100cm^2$. The irradiated animal surface was placed

directly beneath the horn radiating aperture and the entire arrangement enclosed in a microwave-absorbing chamber. This spatially confined the microwave energy and reduced spurious reflections. Microwave power inside and outside of the enclosure were measured using a Narda power density meter to verify the experimental parameters. Vertical movement of the detector probe indicated a voltage standing wave ratio of approximately 1.1 at 2450 MHz in the absence of the experimental animals.

The thermovision system consisted of an AGA camera (model 680), continous gray scale monitor, and color monitor. Absolute temperature measurements were made using the isotherm option in conjunction with a thermal calibration source. Photographic data were obtained using monitors and Polaroid cameras.

Data Acquisition Procedures. Specific experimental procedures were followed for data acquisition to ensure reliable raw data. Test animals were anesthetized using injections of sodium phenobarbital intraperitoneally. The skin area to be examined over both the tumor and normal area was shaved and then a commercial depilatory used to eliminate all hair. Microwave data were obtained by irradiating the examined area for a fixed exposure time, typically 75 s. The resulting surface temperature changes were thermographically measured and photographically recorded after 0, 15, 30, 45, 60 and 75 s. The microwave source was then turned off and thermographic data produced as the skin surface cooled, typically at 60, 120 and 240 seconds after source termination.

For each experimental run an optical photograph, a color thermograph, and a black and white thermograph were made with a Tumor Outline Perimeter Alloy Delineartor (TOPAD) in place. This device was carefully placed and measured in order to associate thermographic data with a particular spatial location on the test animal.

Data Analysis

Raw data is produced in the form of color and black/white Poloraid photographs. The color photographs are presently being manually analyzed. The black/white photographs are analyzed using the aid of digital image processing equipment.

Manual Data Analysis. Different colors on the colored Poloraid photographs represent different temperatures. Analysis therefore consists of converting the colored maps into temperature maps. The temperature for each map region is obtained by noting the calibrated temperature represented by each color. Graphs showing the temporal behavior of tumor tissue and surrounding healthy tissue are produced by observing the color history of points interior and exterior to the tumor, as microwave heating proceeds.

Computer-Aided Data Analysis. Systematic investigations of different tumor types, sizes, and locations in addition to different irradiation frequencies, power levels, and times require the acquisition and analysis of a large volume of raw thermographic data. It has therefore become necessary to incorporate computer aided data analysis techniques to eventually replace the manual techniques used. Techniques have been developed and are in the initial stages of utilization which permit the following: (1) extraction of relevant information from the many thermographic images obtained, (2) thermographic image transformations such as pseudocolor which enhance image structures which otherwise may not be observable, (3) automated determination of suspicious, possible tumor tissue areas.

The images are processed by a system consisting of a vidicon camera and a Comtal image display which are interfaced to a PDP-8 minicomputer. A specialized operating system has been developed to allow either interactive or automatic processing of the images. A sequence of 12 black-and-white thermographic images of a particular examined area are obtained by photographing the thermovision monitor. These images are then digitized by a Spatial Data System digitizer with a resolution of 240 X 256 pixels, with 8 bits of intensity information per pixel. An adjustable micrometer stage is used in conjunction with moveable cursors on the digitizer to register images to be compared to within one pixel. The digitized images are stored on a magnetic disk for subsequent processing.

The initial image in each sequence contains a standard temperature reference and a gray-scale to indicate the temperature range being observed. The temperature is approximately a linear function of the intensity on the thermovision display; however, nonlinearities in both the photographic process and the digitization yield digitized images which are nonlinear, as shown in Figure 2. This nonlinear function is measured for each sequence of images and used to convert each pixel to an absolute temperature. The results indicate a temperature resolution of less thant 0.1°C (compared to 0.5°C without computer analysis).

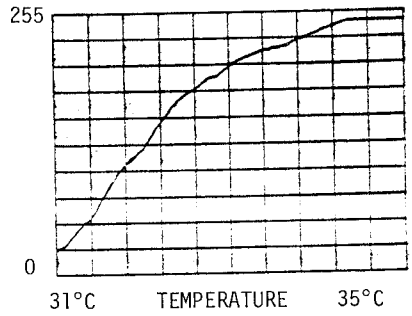


Figure 2. Image intensity as a function of temperature for digitized thermographic images.

After corrections have been made for non-linearities, the average temperatures of the tumor region and four background or healthy tissue regions are calculated for each image in a sequence. These values are saved and automatically plotted as a function of time. The difference between average tumor temperature and the average temperature of healthy tissue is also plotted as a function of time.

To aid in the presentation of thermographic data for technician analysis, a number of processing methods are applied to the images. These can provide a subjective enhancement and reveal details otherwise unobservable. The most dramatic results are obtained by pseudocoloring each image (assigning a unique color to each value of grey). The color assignment can be changed dynamically until one that appears best is obtained. A second method that reveals changes in temperature due to microwave heating is to digitally subtract the image obtained during and after irradiation.

Figure 3 shows a computer produced plot of the temperature distribution of a tumor, where height represents temperature. As the tumor is irradiated this plot changes to provide a graphic illustration of the effects of the microwaves.

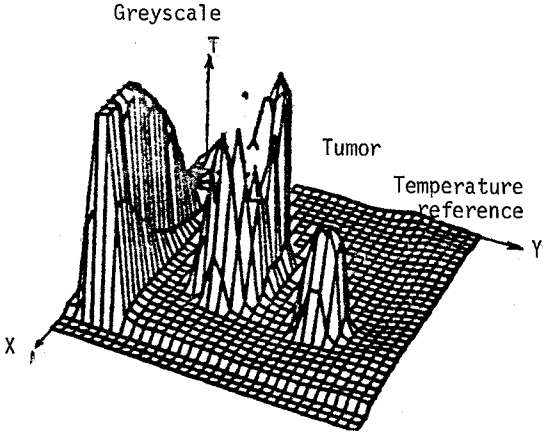


Figure 3. Spatial temperature distribution.

A similar plot can be made after applying spatial derivative operators to the images. These operators calculate spatial temperature differences and are applied over both local and global regions of each image. They thus emphasize either local or global temperature changes. Other local derivative operators useful for measuring image texture have been proposed but not yet applied. It is anticipated that different vascularity in healthy tissue and tumors cause changes in observed thermal image texture which may be emphasized by this technique.

The above techniques can be applied automatically to a sequence of thermograms to yield results which are then interpreted by a technician.

Ultimately, a statistically significant amount of data will be obtained that will allow the correlation of particular image patterns with the presence or absence of a tumor. These patterns will consist of a collection of enhanced images using the techniques described above. The computer will then be able to provide an automated diagnosis.

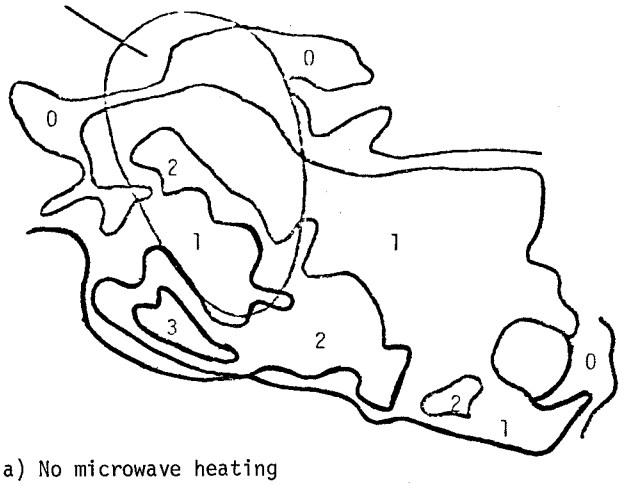
Experimental Results

The experimental results obtained will no be presented. The raw data has thus far been analyzed using manual techniques. Computer results have been obtained which duplicate the results obtained using manual analysis. Examples of the results obtained have been previously discussed and shown in Figures 2-3. Computer analysis is presently only being used to duplicate results obtained manually. Computer analysis will be used exclusively once confidence is obtained in the results.

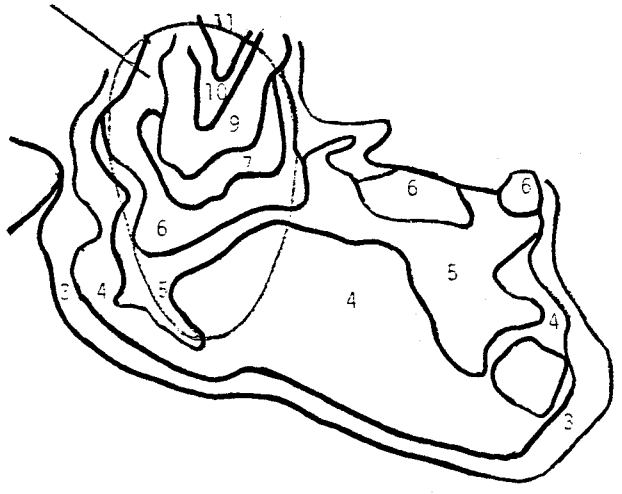
Manually Analyzed Results. Thermographic data have been obtained for guinea pigs and rats with various sizes and types of implanted tumors. Data has been obtained using both 915 MHz and 2450 MHz irradiation frequencies. The data thus far shows that mammary tumors in guinea pigs and rats experience selective microwave heating. Their thermographic visibility is therefore increased. The thermographic visibility of prostate tumors however has not consistently been improved. Representative data illustrating these conclusions will now be presented. Specific data to be presented includes: (1) spatial temperature maps obtained for guinea pigs with 2450 MHz irradiation and (2) graphs of the temporal behavior of tumor and healthy tissue during and after microwave irradiation. Data of this type will be presented for guinea pig and rat tumors irradiated with 915 MHz and 2450 MHz microwaves.

Temperature Maps. Thermographic temperature spatial maps were obtained for guinea pig and rats using 915 MHz and 2450 MHz excitations. Mammary and prostrate tumors of different sizes were used. The prostrate tumor did not consistently experience selective heating. However, mammary tumors did selectively heat such that their thermographic visibility was improve d. Figures 4 (a) and 4(b) illustrate typical rat mammary tumor results obtained for 2450 MHz microwave irradiation. The number zero on each map represents the reference temperature of 31.75°C. Each interger change corresponds to a .5°C. Figure 4 (a) is a representation of the examined tumor bearing region before microwave heating. The thermographic image does not indicate the presence of a tumor in the encircled area. The temperature distribution is observed to be relatively uniform over the entire area. Indeed, portions of the tumor area are

Tumor is encircled



(a) No microwave heating



(b) Microwave heating for 75 seconds.

Map value of 0 corresponds to 31.75°C. Integer increments represent .5°C changes in temperature.

Figure 4. Temperature Map of Tumor Area on Guinea Pig.

colder than the healthy surrounding tissue. However, as microwave energy is added, the tumor selectively absorbs and the observed temperature distribution becomes very nonuniform. The extreme case is shown in Figure 4(b), corresponding to a microwave irradiation time of 75 $s_2$and an energy deposition of approximately 7 J/cm^2. The location of the tumor is clearly evident from this temperature maps and is consistent with the known position outlined. The maximum observed tumor temperature occurred after 75 s of heating and was 31.75 + 5.5°C = 37.25°C. The maximum temperature of healthy tissue away from the tumor was observed to be 31.75 + 2.5°C = 34.25°C. Evidently, the increase in the tumor temperature over that of surrounding healthy tissue is due to selective microwave absorption.

Temporal Response Graphs. Additional information showing the selective tumor heating chararistics can be obtained by observing the temporal behavior of points interior and exterior to the tumor region. These results are shown in Figure 5 for various tumors and excitation frequencies. It can be seen that the mammary tumor/healthy tissue temperature difference increases in time for both excitation frequencies. This is indicative of the selective mammary tumor energy absorption characteristics. The cooling rates for the tumor and healthy tissue are observed to be different, in both cases the cooling rates is relatively slow.

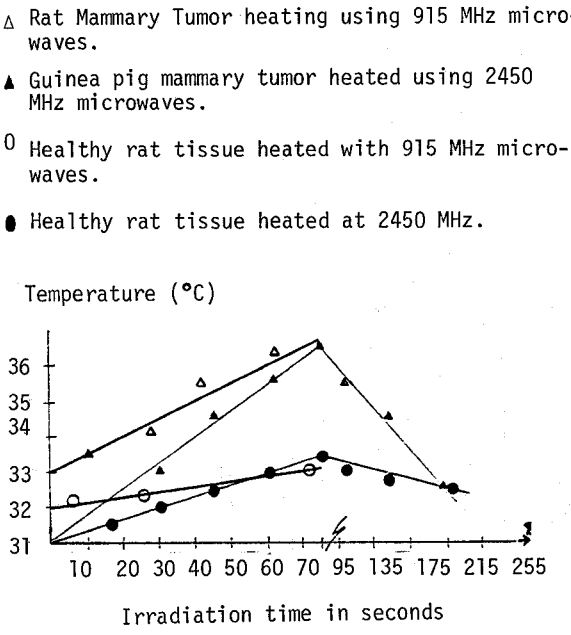


Figure 5. Tumor and Healthy Tissue Microwave Heating and Cooling Temporal Behavior.

Biological Considerations. Two rat tumors used for the experimental thermographic measurements have been examined. These consisted of a rapidly growing mammary adenocarcinoma and a slowly growing prostatic adenocarcinoma. Each tumor is implanted in CDF rats. The rapidly growing tumor is characterized by extensive neovascularization, extreme cellularity with very little fibrous

stroma and a tendency to have necrotic foci. (Figure 6). The prostatic tumor is far less cellular with an appreciable connective tissue stroma. (Figure 7) It is also much less vascular.

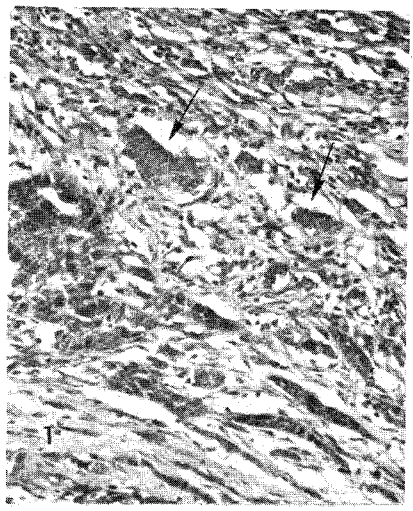


Figure 6. Margin of the mammary tumor and normal tissue. Numerous large vessels are visible (arrows) with nests of tumor cells infiltrating and replacing the normal stroma. In central portions of the tissue little or no stroma is visible. 160x

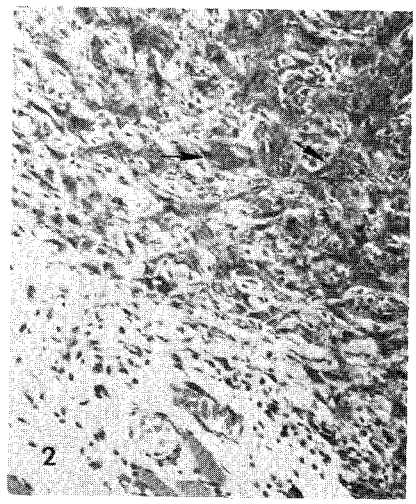


Figure 7. Margin of the prostatic tumor and normal tissue. A few small vessels are visible. The tumor has elicited a slight inflammatory reaction. There is a great deal of tumor-induced stroma within the tumor proper (arrows). 160x

The mammary carcinoma routinely evidences a higher temperature than the normal surrounding tissue before microwave irradiation whereas the prostatic tumor is at about the same temperature as the surrounding tissue. Before microwave irradiation the area of highest temperature of the mammary tumor is a linear region just medial to the tumor, i.e. between it and the vertebral column. This site is also the point of ingress and egress of many of the tumor-induced new blood vessels. The prostatic tumors do not show gross evidence of new large vessels as the mammary tumors do, although clearly the prostatic tumor induces neovascularization, (Figure 7).

In very large mammary tumors there are areas of extensive necrosis and hemorrhage. These areas, although containing stagnant blood, show as colder spots on the thermograms and do not heat up as do areas of tumor free of the large necrotic areas when irradiated. In these hemorrhagic necrotic areas the newly formed vessels generally contain thrombi.

It is clear from these observations that the warmest spots adjacent to the tumors are associated with flowing blood. It is not clear whether this blood is flowing into the tumor and warming, or leaving the tumor having picked up heat from the tumor. Upon microwave irradiation the non-necrotic portions of the mammary tumor heat more rapidly than the normal tissue and more rapidly than the prostatic tumor. The mammary tumor temperature rise is accompanied by an increase in temperature just medial to the tumor, the site of the extensive blood supply. This indicates that the mammary tumor absorbs more energy from the microwaves than the prostatic tumor or the normal tissue and this absorption and dissipation is associated with flowing blood, not stagnant or clotted blood.

There are a number of parameters that distinguish the mammary tumor from the prostatic tumor including blood supply, cellularity and stroma. It is not clear which one or combination of these accounts for the differential heating of the mammary tumor, prostatic tumor and normal tissue, but amount of blood flow appears to be one important parameter. Wet-weight dry-weight ratios, hydroxy proline total protein ratios and DNA protein ratios are being determined in the two tumors and normal skin of rats to determine which correlates best with the differential heating.

Significance and Implications

The results presented show that microwave irradiation of an examined area increases tumor thermographic observability by increasing the temperature gradients. It was observed that the tumor temperature increased by as much as 5.5°C while adjoining healthy tissue increased by only 2.5°C. This made the tumor very obvious using thermovision viewing. It was additionally shown that the heating and cooling rates for the tumor are greater than for healthy tissue. These re-

sults imply that thermographic measurements of the spatial temperature distributions and their temporal behavior resulting from microwave irradiation can be useful for early detection (since detection sensitivity is improved by increasing temperature differentials from approximately 0.5°C to 3°C) and tumor characterization (since the heating and cooling rates are tumor dependent).

Summary and Conclusion

Integrated biological damage resulting from repeated X-ray mammography precludes the use of this technique for mass screening or routine examinations for breast cancer, particularly for younger women. An alternate diagnostic technique which has been used successfully in conjunction with X-ray diagnostics is thermography. However, the sensitivity of this technique is lower than X-ray mammography due to the small surface temperature differential associated with small tumors and the difficulties associated with differentiating between skin surface temperature variations attributable to normal conditions and the presence of tumors. The experiment reported in this paper has, however, shown that the temperature differential between healthy tissue and tumor tissue can be increased substantially by irradiating the examined area with microwave radiation. The increased spatial temperature gradients are then more easily observed using conventional thermographic techniques. This results in an improvement in the sensitivity of the basic thermographic technique. It must be noted, however, that the thermal response associated with all tumors may not be the same as in the case reported here. In particular, the microwave heating profile and the resulting thermographic detectability of smaller and deeper tumors must be investigated before reliable conclusions can be drawn regarding this diagnostic technique. Even so, it seems reasonably certain that if a particular tumor can possibly be detected thermographically, its thermal response can be enhanced by differential heating. Quantitative comparisons between the sensitivity of the microwave-enhanced thermography and X-ray diagnostic techniques, however, cannot be made at the present time. However, the thermographic observability is greatly improved compared to standard thermography for the case reported. The microwave power and required irradiation times are small and result in a maximum healthy tissue temperature increase of only a few degrees Celsius. The technique is therefore not only biologically safe from the standpoint of total microwave energy absorbed, but is also not uncomfortable to the animal being examined.

The thermographic raw data are produced in the form of temperature profile maps. These data are amenable to digital storage and computer manipulation. Various derived data presentations can, therefore, be produced to facilitate decisions, either by man or machine, regarding the presence of tumor tissue. The spatial data obtained have been used to determine the presence and location of a tumor. This is additionally facilitated by observing, thermographically, the temporal behavior of the tumor heating and cooling. These temporal data may prove to be useful in quantifying such tumor characteristics as depth, vascularity, or size.

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