Infrared Imaging in Medicine

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The first documented application of Infrared (IR) imaging in medicine was in 1956 [40], when breast cancer patients were examined for asymmetric hot spots and vascularity in IR images of the breasts. Since then, numerous research findings have been published [24], [41], [44] and the 1960s witnessed the first surge of medical application of the IR technology [20], [23], with breast cancer detection as the primary practice. However, IR imaging has not been widely recognized in medicine nowadays, largely due to the premature use of the technology, the superficial understanding of IR images, and its poorly controlled introduction into breast cancer detection in the 70s [38].

Recently, advances in a couple of related areas have pushed forward series of activities to reappraise the role of IR imaging in medicine [9], [29], [27], [33], [37], [38]. These advances, including the development of the new-generation infrared technology, smart image processing algorithms, and the pathophysiological-based understanding of IR images, will provide a cost-effective, non-invasive, non-destructive, and patient-friendly approach to health monitoring and examination, as well as to assisting diagnosis. In this article, we discuss these new developments in detail.

I. Introduction

Temperature is a long established indicator of health. The Greek physician, Hippocrates, wrote in 400 B.C. "In whatever part of the body excess of heat or cold is felt, the disease is there to be discovered [64]." The ancient Greeks immersed the body in wet mud and the area that dried more quickly, indicating a warmer region, was considered the diseased tissue. The use of hands and thermometers to measure heat-emanating from the body remained well into the sixteenth through the eighteenth centuries. Nowadays, we still reply on thermometers a lot when performing health examination.

All the above-mentioned methods are contact based. Since the British astronomer, Sir William Herschel, discovered the existence of infrared (IR) radiation in 1800, major advances have taken place with IR imaging that do not need direct contact with the patient.

IR radiation occupies the region between visible and microwaves of the spectrum. All objects in the universe emit radiations in the IR region as a function of their temperature. As an object gets hotter, it gives off more intense infrared radiation, and it radiates at a shorter wavelength [33]. The human eye cannot detect IR rays, but they can be detected by using the IR cameras and detectors. Figure 1 illustrates the IR spectral band in finer scale. The boundaries between different IR spectral regions are not agreed upon and can vary. The boundaries that we adopt here are based on references [1], [2], [3], [4], [5].

In general, IR radiation covers wavelengths that range from 0.75μm to 1000μm, among which the human body emissions that are traditionally measured for diagnostic purposes only occupy a narrow band at wavelengths of 8μm to 12μm [66]. This region is also referred to as the *long-wave IR* (LWIR) or *body infrared rays*. Another terminology that is widely used in medical IR imaging is *thermal infrared* (TIR), which, as shown in Fig. 1, covers wavelengths beyond

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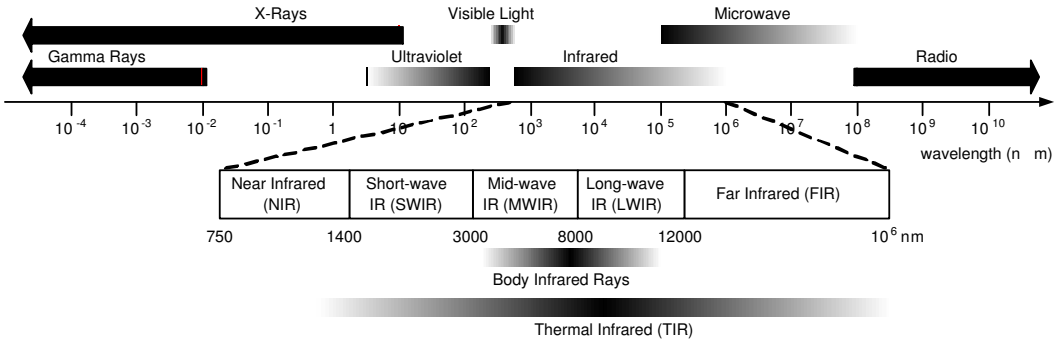

Fig. 1. The electromagnetic spectrum and the IR region.

about 1.4μm. Within this region, the infrared emission is primarily *heat* or *thermal* radiation, and hence the term *thermography*. The image generated by TIR imaging is referred to as the *thermogram*. The near infrared (NIR) region occupies wavelengths between 0.75μm and 1.4μm. The infrared emission that we observe in this region is not thermal [4]. Although the NIR and mid-wave IR (MWIR) regions are not traditionally used in human body screening, the new generation detectors have enabled the use of multispectral imaging in medicine, in which both NIR [46] and MWIR [49] are observed in different diagnostic cases.

In this article, we focus on the discussion of IR imaging in medicine across the full IR spectral region, including the pathophysiological understanding of IR imaging, the development of new generation of IR imagers, and the advanced image processing algorithms of IR images.

II. Pathophysiological-based Understanding of IR Imaging

Infrared imaging is a physiological test that measures the subtle physiological changes that might be caused by many conditions, e.g. contusions, fractures, burns, carcinomas, lymphomas, melanomas, prostate cancer, dermatological diseases, rheumatoid arthritis, diabetes mellitus and associated pathology, deep venous thrombosis (DVT), liver disease, bacterial infections, etc. These conditions are commonly associated with regional vasodilation, hyperthermia, hyperperfusion, hypermetabolism, and hypervascularization [10], [12], [25], [34], [59], [62], [66], which generate higher-temperature heat source. Unlike imaging techniques such as X-ray radiology and CT that primarily provide information on the anatomical structures, IR imaging provides functional information not easily measured by other methods. Thus correct use of IR images requires in-depth physiological knowledge for its effective interpretation.

Take cancer cells as an example which result from permanent genetic change in a normal cell triggered by some external physical agents such as chemical agents, X-rays, UV rays, etc. All types of cancer cells have an imbalanced metabolic activity which leads to the utilization of a large amount of blood glucose and the release of large amounts of lactate into blood. In addition, the high metabolic rate of cancer cells causes an increase in local temperature as compared to normal cells. These factors have enabled IR imaging as a viable technique to visualize the abnormality. The IR image provides more dynamic information of the tumor since the tumor can be small in size but can be fast growing making it appear as a high temperature spot in the IR image [26], [65].

The heat emanating on to the surface from the heat source and the surrounding blood flow can be quantified using the Pennes' bio-heat equation

[54]. This equation includes the heat transfer due to conduction through the tissue, the volumetric metabolic heat generation of the tissue, and the volumetric blood perfusion rate whose strength is considered to be the arterio-venous temperature difference [47]. The equation is given as:

$$k\Delta^2 T - c_b w_b (T - T_a) + q_m = 0 \qquad (1)$$

where k is conductivity, q_m is volumetric metabolic rate of the tissue, $c_b w_b$ is the product of the specific heat capacity and the mass flow rate of blood per unit volume of tissue, T is the unknown tissue temperature, and T_a is the arterial temperature. In theory, given the heat emanating from the surface of the body measured by TIR imaging, by solving the inverse heat transfer problem, we can obtain the heat pattern of various internal elements of the body. Different methods of solving the bio-heat transfer equation have been presented in literature [14], [30]. Although it is possible to calculate the thermal radiation from a thermal body by thermodynamics, the complexity of the boundary conditions associated with the biological body makes this approach impractical.

A. A Sample of Different Interpretation Approaches

Liu et al. [43], [58] presented a new method for analyzing a thermal system based on an analogy to electrical circuit theory; referred to as *thermal-electric analog*. This method does not require a direct solution to the inverse heat transfer problem. It can be used to estimate the depth of the heat source, and furthermore, help understand the metabolic activities undergoing within the human body. The method has been used in early breast cancer detection and has achieved high sensitivity. A diagnosis protocol adopted includes the following six steps:

- Step 1: Growth pattern of lymph nodes in the armpits
- Step 2: Size of the abnormal area
- Step 3: Appearance of the abnormal area
- Step 4: Vascular pattern
- Step 5: Nipples and areola pattern
- Step 6: Dynamic diagnosis with outside agents (antibiotic, etc.)

Another difficulty in IR image interpretation is the lack of standardized image handling procedures. Fujimas did some pioneer work [15] in 1998 by proposing eight thermophysiological expressions to identify abnormal thermogram patterns, referred to as the *thermatomes*.

- Angiological thermatomes: Abnormal temperature regions caused by organic vascular abnormalities
- Functional angiological thermatomes: Abnormal temperature regions caused by vascular disfunctions
- Neuro-dermatomal thermatomes: Abnormal temperature bands caused by somatosensory neuronal disorders
- Myotomal thermatomes: Abnormal temperature regions suspected by abnormal muscular blood flow rate
- Metabolic thermatomes: Abnormal hot and/or cold spots caused by excessive and/or lower heat production and blood flow
- Dynamic thermatomes at environmental temperature stress: Regions with abnormal reactions when a patient received an applied thermal load
- Dynamic thermatomes at medication: Regions with abnormal reactions when a patient is given a medication
- Dynamic thermatomes at various kinds of stress: Regions with abnormal reactions when a patient receives a load (various in type)

To be able to yield objective clinical diagnosis, Anbar et al. [11] proposed the dynamic area telethermometry (DAT) technique. It has been demonstrated to be applicable to any quantitative phthophysiological assessment. The authors demonstrated that using classical Fast Fourier transform (FFT) and elementary statistics, the large amount of sequential observations can be reduced to a single quantitative diagnostic param-

eter without the participation of human experts. Other related work also reported in [16], [22].

We would also like to mention two interesting work conducted recently although their influence on diagnosis is yet to be investigated. Alexjander and Deamer [7] propose to study the sound (rhythms and frequencies) made within the human body through the access of the infrared frequencies of DNA bases. Imagine if we can "hear" the body, would a pleasing pattern to the ear indicate a healthy subject? Or would different patterns present a sign of a certain disease? Through non-linear heat transfer modeling, Pavlidis and Levine [53] show that the periorbital blood flow in anxious states can be used to extract subtle facial temperature fluctuation patterns and thus assist in traditional polygraph examination. Perhaps if we go beyond "imagination", more exciting applications of IR imaging can come into the light.

B. IR Imaging and Early Breast Cancer Detection

Because IR imaging has been mainly used in breast cancer detection since its introduction to the medical field, in the following, we focus on the potential of IR imaging, especially TIR imaging, in *early* breast cancer detection.

According to American Cancer Society's report on Cancer Facts and Figures [61], breast cancer is the most commonly diagnosed cancer in women, accounting for about 30 percent of all cancers in women. In 2004, approximately 215,990 women in the United States receive a diagnosis of invasive breast cancer and 40,110 die from the disease. Figure 2 shows the growth in estimated new breast cancer cases in women since 2001. On the other hand, research [47] has shown that if detected earlier (tumor size less than 10mm), the breast cancer patient has an 85% chance of cure as opposed to 10% if the cancer is detected late. Other research also shows evidence of early detection in saving life [17], [18].

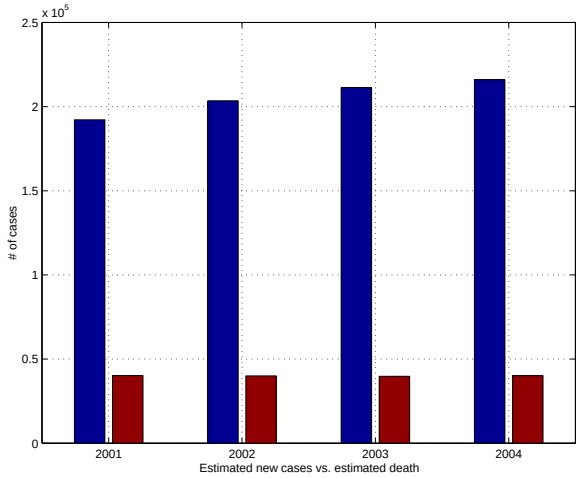

Fig. 2. Estimated new breast cancer cases in women vs. estimated deaths since 2001.

Many imaging modalities can be used for breast screening, including mammography using X-ray, IR, MRI, CT, ultrasound, and PET scans. Although mammography has been the base-line approach, several problems still exist that affect the diagnostic accuracy and popularity. First of all, mammography, like ultrasound, depends primarily on structural distinction and anatomical variation of the tumor from the surrounding breast tissue [38]. Unless the tumor is beyond certain size, it cannot be imaged as X-rays essentially pass through it unaffected. Secondly, the mammogram sensitivity is higher for older women (age group 60-69 years) at 85% compared with younger women (<50 years) at 64% [47] whose denser breast tissue makes it more difficult for mammography to pick up suspicious lesions. Thirdly, patients gone through mammography screening are exposed to X-ray radiation which can mutate or destroy the tissue they penetrate. A new study in the British medical journal (The LANCET [51]) shows that screening actually leads to more aggressive treatment, increasing the number of mastectomies by about 20% and the number of mastectomies and tumorectomies by about 30%. Finally, mammography is relatively expensive nowadays and is less conve-

nient to take (e.g. long duration and uncomfortable contact).

Even though other modalities like MRI and PET scan could provide valuable information to diagnosis, they are not popularly adopted for various reasons including high cost, complexity and accessibility issues [37]. Compared to mammography, MRI, CT, ultrasound, and PET scans which are also called the after-the-fact (a cancerous tumor is already there) detection technologies, IR imaging is able to detect breast cancers 8-10 years earlier than mammography [19], [48]. Keyserlinkg reported in [38] that the average tumor size undetected by IR imaging is 1.28cm vs. 1.66cm by mammography. In addition, IR imaging is non-invasive, non-ionizing, risk-free, patient-friendly, and the cost is considerably low. These features, together with its early detection capability, have enabled IR imaging a strong candidate for complementary diagnostic tool to traditional mammography.

III. New Generation Infrared Technologies

Infrared technology owes its origin to military research and development in the Vietnam era for airborne applications. We focus our discussion on the advances in the detector technologies, especially the uncooled camera development.

A. Cooled vs. Uncooled Thermal Detectors

To some extent, the main factor that determines which wavelengths are included in which infrared region is the type of detector technology used to capture infrared radiation [4]. NIR radiations are observed in very similar way as the visible light, except that special infrared detectors need to be used. On the other hand, TIR imaging generally requires the use of a cooling system in the form of a nitrogen or compressed air cooling bottle, which contains crystals like germanium whose electrical resistance is very sensitive to heat. Due to their size, weight and complexity, these systems were limited to fixed deployment like tripod mounting.

The advance in solid state models has made a new class of sensors possible, the uncooled detector design. The Defense Advanced Research Projects Agency (DARPA) issued a Broad Agency Announcement (BAA) in 1999 [55] that solicits proposals for increasing the performance of the uncooled IR sensors to their theoretical limit. The objective for the thermal sensitivity is set at less than 10 milli-kelvin with a pixel size less than or equal to 25 micrometers. As far as the array size, high-performance arrays for long-range systems can be as large as 960x1280 elements, while arrays for micro-sensors may be as small as 240x320 elements [55].

Two technologies are developed at about the same time to make uncooled sensors a reality, the Barium Strontium Titanate (BST) technology by Raytheon Corporation and the microbolometer technology by Honeywell Corporation.

BST cameras use a ferroelectric detector that converts the infrared energy to a change in *capacitance*. The BST detectors incorporate a mechanical chopper wheel/motor assembly which rotates at 30 times per second during operation to enable the sensor to refresh itself 30 times a second. The images produced can be rather choppy, with dark ghosts produced around hot images and multiple images of the same object smeared across the screen during movement of the camera.

The microbolometer technology, which is thermalelectric in nature, converts infrared energy to a change in *resistance* instead of capacitance as in the BST technology. The microbolometer-based cameras do not require the continuously moving parts and thus can provide high quality images without the choppiness and ghosting associated with the chopper wheel used in BST cameras. The pictures are also smoother and clearer since automatic brightness control instead of mechanical controls is achieved using advanced digital signal processing techniques.

Because the uncooled cameras do not require a cooling system, they are much lighter, smaller, more reliable and less expensive compared to the cooled cameras. Currently, the uncooled cameras are approaching to the thermal sensitivity of the cooled ones (0.05^0C or 0.02^0C of uncool vs. 0.01^0C of cool) and are very popular in breast imaging. Wiecek conducted a brief comparison [67] between uncooled thermal and deeply cooled QWIP (quantum well photodetector) detectors and discussed the limits in both technologies.

B. The Evolution of Other Detector Techniques

Since its first appearance, thermal imager has gone through three generations of development.

The first generation thermal imagers were fielded in the 70s. They use a single detector or small-size linear array detectors. In order to generate the picture, two scanning mirrors are used. This generation imagers generally have the white out problem (or over saturation over high intensity sources). Although mechanical brightness controls are used later to address the problem, the images still lack clarity.

Second generation imagers appeared in the 80s. They use a relatively larger linear array (around 120 elements) or small two-dimensional focal plane array (FPA) (around 64×64 elements) and the scanning mirrors are still used to generate the picture. The most important feature that differs the second generation from the first generation is the employment of the time-delay integration (TDI) technique for image integration and enhancement.

Third generation imagers upgrade the size of the two-dimensional FPA a great deal, some of which contain as many elements as $1,024\times1,024$. In addition, the image processing capabilities are integrated on the FPA, hence the so-called *on-chip image processing*. The third generation does not use mirrors which largely improves the image quality as the less moving part in the camera, the more reliable the system, and the less mechanical noise. Currently, the third generation FPA detectors can capture wavelength from $3-5\mu$m or $8-12\mu$m.

IV. Smart Image Processing Approaches to IR Images

Computer-aided diagnosis (CAD) has been playing an important role in the analysis of IR images, as human examination of images is often influenced by various factors like fatigue, being careless, etc. The detection accuracy is also confined by the limitations of human visual system. On top of all these factors, a shortage of qualified radiologists also put an urgent demand on the development of CAD technologies. Currently, research on smart image processing algorithms on IR images tends to improve the detection accuracy from three perspectives: smart image enhancement and restoration algorithms, asymmetry analysis of the thermogram including automatic segmentation approaches, and feature extraction and classification.

A. Smart Image Enhancement and Restoration Algorithms

One of the problems with thermograms that has put IR imaging in a somewhat disadvantage situation is its lack of resolution due to blur compounded by rather high levels of noise. Snyder et al. [60] developed an algorithm to increase the effective resolution of thermograms by a 2:1 ratio while at the same time removing the noise and preserving edges in the image. This algorithm is based on a minimization strategy known as *mean field annealing*, which takes into account processes of blur, noise, and image correlations, to make an optimal estimate of the missing pixels.

MIT's researchers attempt to enhance the resolution of IR images through another route. The Minimally Invasive Optical Biopsy System developed at MIT [13] uses infrared light in conjunction with an intravenously injected dye and special computer software to create a clear, high con-

trast image that could easily allow physicians to detect breast masses and determine if they are benign or malignant.

In order to eliminate the effect of various thermal environmental conditions, Kakuta et al. [36] developed a "human thermal model" such that IR images taken under different conditions can be compared through normalization of skin surface temperature. The model is based on a numerical calculation of the bio-heat transfer equations and a 16-cylinder-segment model is used as the geometry of the human body.

Kaczmarek and Nowakowski [35] proposed the use of active dynamic thermography (ADT), commonly adopted in nondestructive testing of materials, to further enhance the image quality. ADT analyzes thermal transients after the application of external thermal excitation. Some preliminary results have shown the promise of this approach.

Dynamic thermography is another technique recently proposed to better understand IR images. Because of the interference from complex vascular patterns and the existence of code tumors, in breast cancer detection, researchers have proposed to monitor the thermal recovery process after exposure of cold stress by *sequential* thermography or by digital subtraction thermography. Studies [50] have shown an increase in sensitivity of breast imaging.

B. Asymmetry Analysis

Making comparisons between contralateral images are routinely done by radiologists. When the images are relatively symmetrical, small asymmetries may indicate a suspicious region. This is the underlying philosophy in the use of asymmetry analysis for mass detection in breast cancer study [21] as well as in anomaly detection of other parts of the human body. Unfortunately, these small asymmetries might not be easy to detect and it is important to design an automatic approach to eliminate human factors. There have been a few papers addressing techniques for asymmetry analysis of mammograms [21], [68], [69].

Head et al. [28], [42] recently analyzed the asymmetric abnormalities in IR images. In their approach, the image is segmented first by operator. Then breast quadrants are derived automatically based on unique point of reference, i.e. the chin, the lowest, rightmost and leftmost points of the breast. Qi et al. [57] developed an automatic approach to asymmetry analysis in IR images. It includes automatic segmentation and pattern classification. Hough transform is used to extract the four feature curves that can uniquely segment the left and right breasts. The feature curves include the left and the right body boundary curves, and the two parabolic curves indicating the lower boundaries of the breasts. Mabuchi et al. [45] designed a computerized thermographic system, which would produce images of the distribution of temperature differences between the affected side and the contralateral healthy side. Because there is no standard skin surface temperature existed, the system measures the body-surface temperature of each pixel in the affected area and subtract from it the body-surface temperature of the corresponding pixel in the symmetrically located contralateral healthy area to generate the difference image.

C. Feature Extraction and Classification

Upon segmentation, different features can be extracted from the segments. Asymmetric abnormalities can then be identified based on mature pattern classification techniques. In this process, feature extraction is crucial to the success of computer-aided diagnosis. [39] shows that the high-order statistics (e.g. variance, skewness, and kurtosis) and joint entropy are the most effective features to measure the asymmetry, while low-order statistics (e.g. mean) and entropy do not assist asymmetry detection. Jakubowska et al. [32] also addressed the importance of using statistical parameters (1st and 2nd order) in extracting thermal signatures for asymmetry analysis.

Szu et al. [63] proposed a new paradigm shift that uses at least two dual-band (mid and long) infrared imaging cameras operating simultaneously on the patient. This system enables a smart brain-like neural network algorithm, the Lagrange Constraint Neural Network (LCNN), to achieve sub-milimeter scaling of the close-up breast imaging for the vascular and angiogenesis effects as well as stage-zero detection of ductal carcinoma in situ.

The above mentioned techniques are just samples of activities reported in recent conferences, workshops and symposia. Another trend of effort that is worth mentioning is the transition of automatic target recognition (ATR) algorithms developed for military application to medicine. "From tanks to tumors" [31], [52] has been the theme of this transition and the rich collection of ATR algorithms that the military has sponsored will greatly improve the state-of-the-art of CAD development.

V. Concept Validation

Concept validation is an important procedure in the promotion of IR-based breast screening where blind diagnosis and clinical evidence are necessary. Although there have been a lot of clinical trials conducted so far [8], there has not been a well-designed, standard database created for the purpose of concept validation.

The Advanced Concept Analysis, Inc. located at Falls Church, VA was awarded in 2000 to manage the creation of such a database. The project is sponsored by the Deputy Assistant Secretary of the Army for Installations and Environment (Environmental Safety and Occupational Health), the Office of the Deputy Undersecretary of Defense for Science and Technology (ODUSD/S&T), the Air Force Research Laboratory (AFRL), and the Office of Naval Research (ONR). An Internet-based Virtual Distributed Laboratory (VDL) at AFRL will house over 8,000 images from over 2,000 patients provided by E.H.H. Breast Cancer Research and Treatment Center, Baton Rouge, LA and Ville Marie Medical Center & Women's Health Center, Montreal, Canada. Each center will use the collaboration tools and evaluation procedures on the VDL to conduct *blind* diagnoses of the images provided by the other. Blind test results will be compared with actual clinical evidence stored with the imagery. VDL access may be applied for at [6].

VI. Summary

This article discussed recent research achievements in medical theomography with a focus on early breast cancer detection. The objective is to show that due to the advances in infrared technology, image processing techniques, and the pathophysiological-based understanding of theromograms, IR imaging is mature to be used as a first line supplement to both health monitoring and clinical diagnosis. We have established a website [56] to facilitate researchers working in the field of medical thermography to exchange research findings. We welcome contributions to enrich this list of collections.

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