Potential of thermal imaging as a tool for prediction of cardiovascular disease

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ABSTRACT

Vascular dysfunction is associated with onset of cardiovascular disease (CVD). Its effect is reflected as temperature change on the skin. The aim of this work was to test the potential of thermal imaging as cost effective screening tool for prediction of CVD. Thermal imaging of various parts of the subject (N = 80, male/female = 44/36, aged 25-75 years) was done using noncontact infrared (IR) camera. In each subject, total cholesterol (TC; mg/dl) and high-density lipoprotein (HDL, mg/dl) were measured according to standard biochemical analysis. Based on National Cholesterol Education Program ATP III criteria, subject with known CVD (N = 16) and age- and sex- matched normal subjects (N = 21) were included in the study. The average surface temperature of various parts from head to toe was calculated and statistical analysis was performed between the groups. In the total population (N = 37), correlation study shows TC (mg/dl) was correlated with measured surface temperature of the following regions: Temporal left (r = −0.316) and right (r = −0.417), neck left (r = 0.347) and right (r = −0.410), and hand left (r = 0.387). HDL (mg/dl) was found to be correlated with measured surface temperature of the following regions: Temporal left (r = 0.445) and right (r = 0.458), hand left (r = 0.470), and foot anterior left (r = −0.332) and right (r = −0.336). Temperature asymmetry was more significant in upper extremity in CVD group. Using the surface temperature, regression models were calculated for noninvasive estimation of TC and HDL. The predictive ability of measured surface temperature for TC and HDL was 60%. The model for noninvasive estimation gave sensitivity and specificity value of 79 and 83% for TC and 78 and 81% for HDL, respectively. Thus, the surface temperature can be one of the screening tools for prediction of CVD. The limitation of the present study is also discussed under future work.

Key words: Cardiovascular disease; framingham score; infrared imaging; lipid profile; thermal imaging; vascular dysfunction

Introduction

Every year, 17.1 million lives are claimed by the global burden of heart disease and stroke. By 2020, the World Health Organization (WHO) estimates nearly 25 million cardiovascular disease (CVD) deaths worldwide. This noncommunicable disease is emerging as major causes of death in India. Estimate by WHO indicates that 50% of death and disability from CVD can be reduced by a combination for simple effective national efforts and individual actions to reduce major risk factors. The traditional approaches for diagnosis of the disease is by monitoring of biochemical markers like total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, or by in vivo techniques like ultrasound, magnetic resonance imaging, or computed tomography. Atherosclerosis is the major cause of CVD,[1] where the disturbances to blood flow causes temperature variation in skin surface. Blood parameters that are involved in lipid metabolism are HDL and LDL. The important role of HDL is to aid in uptake of cholesterol from peripheral tissues to liver through the reverse cholesterol transport.[1] Thus antiatherogenic mechanism of HDL which removes excess of cholesterol from blood vessel wall prevents the stenosis of blood vessel due to atherosclerosis, specifically in the peripheral vessels.[2] Hence, low level of HDL (<40 mg/dl) is strongly associated with an increased risk of CVD.[3,4] This vascular dysfunction alters the skin temperature making temperature as an important indicator of health.[5] Thermal imaging is one of the methods involving nonionizing radiation, which can be used for diagnosis of CVD. Ultrasound Doppler
measurement, one of the techniques for diagnosis of plaque is more operator dependent and accurate measurements are possible only if blood vessel is perpendicular to the transducer. Thermal imaging is a cost-effective tool, which can be used to analyze the physiological function. It is based on nonionizing radiations with sensitivity of 0.05°C. Invasive noncontact thermography has emerged as a useful tool in elaborating the pathophysiologic features of atherosclerosis and other related diagnosis like deep vein thrombosis. Hence, this study was carried out as preliminary study to establish the correlation between the CVD biochemical markers and the surface temperature of the human body.

**Infrared Imaging**

Thermal imaging captures the natural IR radiation from our body. The main attraction of thermal imaging comes from the facts that it is completely noncontact, therefore giving no interaction with tissues, easy to use, and easy to store the data. It is one of the simplest forms of imaging which can give physiological information. Hence, it can be used to diagnose disorders connected with musculoskeletal conditions, peripheral/cephalic vascular conditions, diagnosis of cancer/tumor, deep vein thrombosis, and facial vasculature recognition for biometric purpose. According to Madjid. M et al., temperature difference was observed between atherosclerotic plaque and healthy vessel wall by thermography. The recent development of multimodal four-dimensional (4D) dynamic thermal imaging can give an early prediction of many medical conditions. A variety of disorders in face, skull, and neck can give a good thermal signature, hence blood flow is under a thin layer of tissue. According to Planck’s law, the dry skin, nearly an ideal black body (emissivity 0.98), is a long wave IR radiator with a maximum emission at about 10 μm. The surface of the skin is heated by the blood vessels that lie close to it. The human body is considered to be a stairway of heat with highest temperature in forehead and cervical regions, followed by trunk, and then decreasing over the limbs. Thus, thermal imaging of the skin can give sufficient information regarding the vascularity below the skin. If blood flow is mechanically obstructed in a vessel, blood will flow through it, reduced or completely occluded, making it appear cooler than normal or vice versa.

The human thermal system maintains a core body temperature of 36.7°C. Any deviation from this causes considerable discomfort. The heat generated by metabolic activities is conducted through bone, tissue, and skin. The large arteries and veins also play a major role in transferring the temperature to maintain thermal comfort of the human system.

Atherosclerosis, the major cause of CVD is a chronic inflammatory condition of the blood vessel wall. The asymptomatic atherosclerosis causes variation in blood supply and thereby affects the surface temperature pattern. Ley and Kim have demonstrated that there is a hotspot at the site of atherosclerotic lesion. Yu et al. have demonstrated that rise in temperature has been observed at the site of inflammation in arteries of rabbit, which leads to change in temperature pattern. The authors have proved that the difference in temperature has been observed even before there is no clinical sign of inflammation. The intimal surface temperature has been correlated with increase in cell density as atherosclerotic progresses. Hence, IR-based measurements were proposed by Honda et al., for vascular studies. Using thermal imaging for face recognition application is based on the fact that thermal image has the ability to capture the superficial blood vessel patterns very effectively. Thus, the surface temperature of the skin can be a good indicator of health.

**Materials and Methods**

**Study participant**

A free screening camp for CVD was organized at a private hospital during March 2010 and a subsequent medical camp in May 2011. Out of the 150 registered participants, 80 were recruited for the study. A total of 80 subjects, aged above 25-70 years participated in the study. The core temperature of all the subjects was measured using thermometer. Any known cases of fever, neurological disorders, diabetes mellitus, thyroid abnormalities, and nephropathy were excluded from the study. A detailed questionnaire prepared for the study was used to evaluate the health status of the subjects, participated in the camp. An informed consent form was obtained from all the subjects. This clinical trial was also registered in the Clinical Trial Registry of India (Ref. No. Reg/2012/06/005696). The anthropometric measures like body weight, body height, blood pressure, and waist and hip circumference were measured in each one of the subject.

**Biochemical analysis**

Blood samples were taken in all subjects (N = 80) in nonfasting condition. The following parameters: i) TC (mg/dl), ii) HDL (mg/dl), and iii) HbA1c (%) were measured for each subject according to the standard biochemical analysis.

**Study group**

In this study, National Cholesterol Education Program ATP III criteria for CVD were used to classify the subjects, who participated in the study. It is quoted in many studies involving Asian Indians. According to this, a subject with low level of HDL (<40 mg/dl) and higher level of TC (>200 mg/dl) was considered as having CVD problem. On the other hand, subject who had normal levels of both HDL and TC was considered as normal one. After the inclusion and exclusion criteria, total number of subjects included in the study was 37, and the subjects were classified as follows:
• Group-I: CVD: \( N = 16 \), male/female (M/F) = 10/6, mean (± SD) age = 50 (± 10.56) years. Subjects with low level of HDL and higher level of TC
• Group-II: Normal: \( N = 21 \), M/F = 12/9, mean (± SD) age = 53 (± 10.27) years. Subjects with normal levels of HDL and TC.

**Framingham CVD risk score**

Framingham cardiovascular risk score (2008) is an algorithm based on the Framingham Heart Study for determining individual's CVD risk.\(^{[19,20]}\) For each patient in the study population, the Framingham general cardiovascular 10-year risk score based on the Framingham Heart Study was computed using his/her age, gender, smoking habit, TC, and HDL values to ensure the severity of the disease in the study population selected. The score for normal group (10.2%) falls into low risk category, whereas, CVD group is at an intermediate risk (17.9%).

**Thermal profile**

A systematic protocol as proposed by the International Association of Certified Thermographers was maintained for capturing the thermal images.\(^{[21]}\) The clinical trial was conducted in special metabolic clinical trial ward constructed under Good Clinical Practice regulation, where the room temperature was maintained at 20°C. All the subjects were made to sit for 15 min in the temperature-controlled waiting room. This reduces the effect of an environment temperature on the skin. The subjects were then asked to stand in the image capturing room uncovered below knee, no metal ornaments of any kind in hand or face. The relative humidity was 50% and emissivity was set at 0.98. The trial was conducted for a period of a week in the forenoon session only, to avoid the effect of cyclic variations in the atmospheric temperature in the study. An IR camera (Therma Cam T400, FLIR Systems, USA) was used to acquire thermal image of the following parts of the whole body in each subject under standard conditions: i) temporal (left and right), ii) neck lateral (left and right), iii) upper and lower arm (left and right), iv) leg (left and right), and v) foot (left and right). FLIR T400 IR camera has an option of internal calibration that can be performed when needed. The camera calibration program uses temperature references that are calibrated annually and traceable to the National Institute of Standards of Testing. The distance between camera and subject was kept 50 cm constant. All the subjects underwent single imaging session. The images were stored and then analyzed offline using the software FLIR Quick report, version 1.2. A series of 14 region of interest (ROI) were selected using automated area tool in FLIR. Maximum area was selected in all the regions avoiding the background. The rectangle select tool available with the software was used and care taken to have an almost uniform area while selecting the ROI for measurement. The average temperature displayed by the software was considered for analysis.

**Statistical analysis**

The normalization of the data was checked using the Shapiro–Wilk test which gave a greater significance value (\( P > 0.05 \)). Pearson's correlation analysis was done between the biochemical parameters and the average temperatures measured in various regions of the total populations. Independent Student’s \( t \)-test was employed to compare the mean of the biochemical parameters and the average temperatures measured among the groups. The contribution of the temperatures predicting noninvasively TC and HDL values were tested by performing multiple regression analysis. All the tests were carried out by Statistical Package for Social Sciences (SPSS) software, version 17.0 (SPSS Inc, Chicago, Illinois).

**Result**

**Correlation between biochemical parameter and surface temperature**

In total population (\( N = 37 \)), the measured TC (mg/dl) was found to be correlated with the measured surface temperature of the following parts of the whole-body: i) temporal left (\( r = -0.316, P < 0.05 \)), ii) temporal right (\( r = -0.417, P < 0.05 \)), iii) neck left (\( r = 0.347, P < 0.05 \)), iv) neck right (\( r = -0.410, P < 0.05 \)), and v) hand left (\( r = 0.387, P < 0.05 \)). Further measured HDL (mg/dl) was found to be correlated with measured surface temperature of the following parts of the whole body: i) Temporal left (\( r = 0.445, P < 0.05 \)); ii) Temporal right (\( r = 0.458, P < 0.05 \)); iii) Hand left (\( r = -0.470, P < 0.05 \)), iv) foot anterior left (\( r = -0.332, P < 0.05 \)), and v) foot anterior right (\( r = -0.336, P < 0.05 \)). Figures 1 and 2 shows the correlation of TC with temporal right temperature and HDL with hand left temperature, respectively.

**Comparison of clinical variables among the group**

From the Table 1, it was observed that there was no significant difference in mean age (years) of the subjects between normal and CVD groups. Also, there was no statistically significant difference in HbA1C level in both groups. In the diseased group, both the clinically evaluated mean values of Framingham CVD risk score and systolic blood pressure (BP; mmHg) were greater (\( P < 0.05 \) and \( P < 0.01 \), respectively), compared to its normal counter parts.

**Comparison of mean surface temperature among the groups**

The analysis of the average surface temperature in various parts of the body was indicated that a greater difference in
temperature was observed in foot. The average temperature difference between the groups in upper extremities is about 1%, whereas, the same lower extremities was about 8% with a highest temperature difference of about 9.4% in foot posterior right as shown in Table 2.

**Asymmetry analysis**

Under normal circumstances, the temperature of the surface of the human body is symmetrical about the anatomical medial axis. In the normal group, higher symmetrical surface temperatures on both left and right side of upper and lower body regions were observed, when compared to CVD group [Table 3]. On the other hand, in the diseased group, a statistically significant asymmetrical surface temperature difference were observed in hand (2%, \( P < 0.001 \)) and temporal regions (1%, \( P < 0.05 \)).

**Multivariate regression analysis**

The predicting ability of the thermal imaging in diagnosing CVD disease was tested using the regression analysis. The whole-body region surface temperatures which correlated with HDL and TC were used in the prediction model to calculate sensitivity and specificity. A stepwise linear multiple regression was conducted to evaluate whether all the variables (that was correlated with TC and HDL) are necessary. Those variables which gave statistically insignificant contribution to model were removed. As shown in Tables 4 and 5, the models with highest \( r^2 \) value were selected to frame the equation. The equations are listed as follows:

\[
\text{HDL (mg/dl)} = 8.197 - 3.368 \times X_1 - 3.124 \times X_2 + 0.661 \times X_4
\]

**Table 1: Statistical analysis of biochemical parameters**

| Variables               | Normal (N=21) | CVD (N=16) | P value |
|-------------------------|---------------|------------|---------|
| Age (years)             | 24 ± 10.27    | 35 ± 10.56 | NS      |
| Height (cm)             | 156.39 ± 8.63 | 159.15 ± 9.19 | NS     |
| Weight (kg)             | 62.87 ± 10.89 | 68.85 ± 10.21 | NS      |
| Framingham risk score (%) | 9.2 ± 8.77   | 7.9 ± 7.82 | <0.05   |
| Waist circumference (cm) | 89.00 ± 15.17 | 91.63 ± 4.96 | NS      |
| Hip circumference (cm)  | 98.00 ± 13.48 | 98.63 ± 5.45 | NS      |
| Systolic BP (mmHg)      | 123.04 ± 14.60 | 134.29 ± 16.51 | <0.01   |
| Diastolic BP (mmHg)     | 81.22 ± 9.70  | 84.29 ± 9.38 | NS      |
| TC (mg/dl)              | 177.78 ± 44.90 | 222.70 ± 51.43 | <0.01   |
| HDL cholesterol (mg/dl) | 42.63 ± 8.02  | 54.92 ± 1.27 | <0.01   |
| TC/HDL                  | 4.23 ± 0.90   | 5.49 ± 1.98 | <0.01   |
| HbA1C (%)               | 6.80 ± 2.05   | 7.45 ± 1.98 | NS      |

**Table 2: Statistical analysis of average surface temperature in major regions**

| Measured surface temperature at different ROI | Normal (N=21) (°C) | CVD (N=16) (°C) | Difference in temperature (°C) | P value |
|---------------------------------------------|---------------------|----------------|-----------------------------|---------|
| Temporal left                               | 33.78 ± 0.63        | 33.59 ± 0.67   | 0.5                         | <0.05   |
| Temporal right                              | 34.11 ± 0.57        | 34.59 ± 0.91   | 0.79                        | <0.01   |
| Neck left                                   | 34.56 ± 0.52        | 35.31 ± 0.9    | 0.03                        | <0.05   |
| Neck right                                  | 34.06 ± 0.58        | 35.04 ± 0.9    | 0.51                        | <0.01   |
| Hand left                                   | 32.5 ± 0.64         | 34.68 ± 1.03   | 0.65                        | <0.05   |
| Hand right                                  | 32.44 ± 0.68        | 33.99 ± 0.97   | 0.1                         | NS      |
| Leg left                                    | 33.3 ± 0.7          | 33.24 ± 0.99   | 0.04                        | NS      |
| Leg right                                   | 32.17 ± 0.63        | 33.19 ± 1.03   | 0.06                        | NS      |
| Foot anterior left                          | 27.42 ± 0.45        | 31.73 ± 1.81   | 2.37                        | <0.01   |
| Foot anterior right                         | 27.28 ± 0.46        | 31.78 ± 1.92   | 2.33                        | <0.01   |
| Foot posterior left                         | 25.70 ± 0.54        | 30.07 ± 2.74   | 2.51                        | <0.01   |
| Foot posterior right                        | 25.40 ± 0.55        | 30.13 ± 2.65   | 2.60                        | <0.01   |

NS: Not significant, ROI: Region of interest, CVD: Cardiovascular disease
TC (mg/dl) = 626.39 - 10.58*X_2 + 46.55*X_4 - 47.24*X_5 [From step 3, Table 5].

Where
• X_1 - Surface temperature of hand left (°C)
• X_2 - Surface temperature of temporal right (°C)
• X_3 - Surface temperature of neck left (°C)
• X_4 - Surface temperature of foot anterior right (°C).

Validation of regression results
Using the obtained regression equations; HDL and TC were predicted for the population studied. Then, paired sample’s t-tests were conducted to compare both biochemically measured HDL and TC values with their corresponding predicted values. There was no statistically significant difference between the measured and predicted HDL values (t = 2.02, P = 0.54). Similarly, there was no statistically significant difference between the measured and predicted TC values (t = 2.02, P = 0.98). The model gave sensitivity and specificity values as 78 and 81% for HDL and 79 and 83% for TC, respectively.

Discussion
Correlation analysis shows that there was a significant increase in temperature in neck left, hand left, leg left, and foot anterior and posterior region when compared to the CVD clinical biomarkers. It has been concluded by Rubinstein and Sessler[25] that skin temperature gradient are an accurate measure of thermoregulation, especially in peripheral vasculature. TC, a fatty substance, if in excess causes deposition on the vessel walls affecting the circulation. HDL removes the excess cholesterol in the blood and helps in the process of eliminating it by sending to liver. Hence, higher the value of HDL, less the chances of forming blockages in blood vessel and more uniform circulation can be achieved.[23]

Claudication due to impaired circulation is due to plaque formation.[24] The subclavian artery and brachiocephalic arteries are cited as the most common early site of atherosclerotic lesions in the upper extremity.[25] The lesions tend to alter the blood flow. Hence, the difference in correlation of the biomarkers (TC and HDL) with surface temperature of hand and neck between the left and right side confirms the same.

Blood pressure asymmetry especially in upper extremity is a common early symptom in clinical examination of atherosclerosis.[26] The pulse asymmetry depends on the extent of degree of stenosis. Blood flow through ulnar artery is a confirmatory test for occlusive diseases of the upper extremity.[25] In a perspective study, Juha et al., have evaluated the surface temperature asymmetry in leg for subjects who were at high risk of peripheral arterial disease.[30,31] Vascular asymmetry is clearly depicted in the hand of CVD group with both temperature asymmetry and difference in mean temperature between the normal and CVD group.

The extent of vascular stenosis is judged by the examination of lower extremity. Sanjeev et al., have established that if the stenosis is prolonged and not supervised, then the lower extremity blood pressure is a representative of central aortic root pressure.[28,29] Compared to ankle brachial pressure index (ABI), the foot pulses from dorsalis pedis and posterior tibial pulses were found to be more accurate in detecting the arterial disease in lower extremity as reported by Armstrong et al.[30] The significant difference in mean temperature in lower extremity, foot anterior and posterior region (8% difference, P < 0.001) was obtained while comparing the normal and CVD group confirms the same. Figure 3 is a right and left hand of normal subject (age: 52 years) with temperature symmetry. Figure 4 is hand of CVD subject (age: 55 years) showing temperature asymmetry in the palm region. The

Table 3: Asymmetry analysis of surface temperature

| Different ROI of whole body | Difference in mean surface temperature between left- and right-side region | Normal (N=21) | CVD (N=16) |
|----------------------------|--------------------------------------------------------------------------|-------------|-----------|
|                            | %                         | P value     | %               | P value     |
| Temporal                   | 0.23                      | NS          | 1.9               | <0.05       |
| Neck                       | 0.06                      | NS          | 0.43             | NS          |
| Hand                       | 0.15                      | NS          | 2.0               | <0.001      |
| Leg                        | 0.15                      | NS          | 0.15             | NS          |
| Foot anterior              | 0.11                      | NS          | 0.15             | NS          |
| Foot posterior             | 0.18                      | NS          | 0.20             | NS          |

NS: Not significant, ROI: Region of Interest, CVD: Cardiovascular disease

Table 4: Step-wise regression models with HDL as dependent variable

| Step-wise analysis   | HDL as dependent variable | Intercept/ independent variables of surface temperature | Coefficients | Standard error | P value |
|----------------------|----------------------------|-------------------------------------------------------|--------------|----------------|---------|
| 1 (r²=0.217, adjusted r²=0.194 at P<0.001) | Constant                    | -57.19                                                | 29.96        | 0.06           |         |
|                      | Hand left                   | 2.675                                                 | 0.872        | 0.00           |         |
| 2 (r²=0.520, adjusted r²=0.491 at P<0.001) | Constant                    | 39.34                                                 | 31.81        | 0.23           |         |
|                      | Hand left                   | 3.298                                                 | 0.706        | 0.00           |         |
|                      | Temporal right             | -3.37                                                 | 0.737        | 0.00           |         |
| 3 (r²=0.605, adjusted r²=0.568 at P<0.001) | Constant                    | 8.19                                                  | 31.65        | 0.79           |         |
|                      | Hand left                   | 3.37                                                  | 0.651        | 0.00           |         |
|                      | Temporal right             | -3.12                                                 | 0.69         | 0.00           |         |
|                      | Foot anterior right        | 0.66                                                  | 0.25         | 0.01           |         |

HDL: High-density lipoprotein
upper extremity temperatures especially of hand left also contributes significantly (P < 0.001) to prediction of both TC and HDL as indicated by the regression models. Figure 5 is face of normal female (age: 45 years) subject showing temperature symmetry. Figure 6 is a female subject (age: 49 years) whose left temporal region shows high temperature (35.9°C) compared to the right side as indicated within the markers.

**Limitations of our study**

Several limitations of our study should be mentioned. First, the trial was conducted for a period of a week in the forenoon session to avoid the effect of cyclic variations in the atmospheric temperature. Hence, out of the 150 registered participants, only 80 were recruited for the study. After implementing the appropriate inclusion/exclusion criteria, the study population reduced to 37 subjects. Hence, the trial has to be concluded as pilot study. Second, statistical conclusion could be drawn, but correlation relation between surface temperature and TC/HDL is region-specific, which makes the general surface temperature inconclusive for CVD subjects. Third, confirmatory tests like measurement of ankle/brachial index and biochemical parameters like LDL-cholesterol, triglycerides, urinary protein, and urinary glucose was not done to differentiate atherosclerotic and nonatherosclerotic CVD subjects. Last, the reproducibility of the measurement has to be checked by repeating the imaging session after few days.

**Conclusion**

For the study population selected, the average temperature in various ROI was calculated using the FLIR software. The statistical analysis was performed on the clinical parameters, average temperature measured, and the

![Figure 1: Correlation of measured total cholesterol (TC; mg/dl) with surface temperature (°C) of temporal right region](image1.png)

\[ y = -0.007x + 36.34 \]
\[ R^2 = 0.180 \]

![Figure 2: Correlation of measured high-density lipoprotein (HDL; mg/dl) with surface temperature (°C) of hand left region](image2.png)

\[ y = -0.0621x + 37.233 \]
\[ R^2 = 0.1951 \]

![Figure 3: Right and left hand of normal male subject with TC = 151 mg/dl and HDL = 49 mg/dl, temperature symmetry in the palm region can be observed clearly](image3.png)
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The key findings of this work are: First, the correlation of the parameters TC and HDL with the sites of commonly affected arteries in the upper and lower extremity. Secondly, mean difference in surface temperatures of lower extremities indicating the presence of stenosis can be a diagnostic criterion apart from the usual ABI method for the diagnosis of peripheral arterial disease. Third, the temperature asymmetry similar to blood pressure asymmetry which is observed in the upper extremity can be an early symptom of arterial occlusive disease. The regression equation formed can be used for predicting the HDL and TC values noninvasively.

Future work

In a large-scale study, various approaches like static and dynamic IR imaging and advanced image feature extraction techniques with subsequent development of automated computer-aided diagnostic model can be done. This will bring out the potential of thermal imaging for predicting CVD with more sensitivity in a clinical setup.

Acknowledgment

We would like to thank Dr James Pandian, Dean, SRM Medical College Hospital and Research Centre, Kattankulathur, Chennai, India for his clinical advice and IGCAR Kalpakkam, Chennai, India for all their support during the study.

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How to cite this article: Thiruvengadam J, Anburajan M, Menaka M, Venkatraman B. Potential of thermal imaging as a tool for prediction of cardiovascular disease. J Med Phys 2014;39:98-105.

Source of Support: Nil, Conflict of Interest: None declared.