Cold provocation improves breast cancer detection with IR thermography - A pilot study

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Lääketieteen yksikkö
Rintasyövän infrapunakuvantaminen
Maaliskuu 2014

Tampereen yliopisto

Lääketieteen yksikkö

Lääperi Eero: Cold provocation improves breast cancer detection with IR thermography - A pilot study

Kirjallinen työ

Ohjaaja: dos. Prasun Dastidar

Toukokuu 2013

Avainsanat: kuvantaminen, seulonta, infrapunakamera

Infrapunakuvausta on tutkittu apuvälineenä rintasyövän havaitsemiseksi. Aiemmat tutkimukset ovat antaneet lupaavia tuloksia. Tässä tutkimuksessa käytettiin kylmäprovokaatiota ja liikkeenkorjausta kuvaustuloksen parantamiseksi.

Tutkimuksessa käytetty potilasaineisto oli röntgenkuvilla ja histologialla varmistettuja rintasyöpäpotilaita. Tutkimuksessa olleista yhdeksästä potilaasta kolme soveltui tähän tutkimukseen. Käytetty kamera oli Lodzin yliopistossa kehitetty mikrobolometrinen viilentämätön IRvox384 infrapunakamera. Rintoja viilennettiin kylmäpakkauksella 15 s ajan, jonka jälkeen kuvattiin 300 kuvan sekvenssi kahden sekunnin välein. Kuvasarjojen liikeartefaktaa vähennettiin liikkeenkorjausohjelmistolla. Saadut tulokset sovitettiin ihmisen iholle sopivaan yhtälöön, josta saatuja terveen ja sairaan alueen aikavakiota vertailtiin toisiinsa.

Kasvainten alueella havaittiin olevan korkeampi aikavakio kuin terveellä alueella. Tämä tarkoittaa, että kasvaimen alueella ihon normaalin lämpötilan palautuminen kestää kauemmin kuin terveellä alueella.

Korkeamman aikavakion esiintyminen kasvainalueilla täytyy varmentaa suuremmalla rintasyöpäpotilasjoukolla ja kuvaustapahtumalle täytyy vakioida tarkat toimintatavat, jotta toistettavuus paranisi ja infrapunakuvausta voitaisiin harkita mahdollisena seulontatyökaluna.

Cold provocation improves breast cancer detection with IR thermography- A pilot study

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SUMMARY

BACKGROUND: Previous studies applying infrared thermography for breast cancer detection have shown promising results.We assumed that the reaction for cold provocation differs in healthy and cancerous tissue. In this study we used cold provocation and movement correction in order to enhance the result.

MATERIALS AND METHODS: The cancer patients for the study are from a preliminary investigation made in Tampere University hospital. Three out of nine patients examined were suitable for this study. We used a microbolometric uncooled camera IRvox384 thermal camera developed at Technical University of Lodz for medical applications. We cooled the breasts for 15 seconds and then a sequence of 300 images was recorded with the frame rate of 2 frames per second. The total recording time was 150 s.

RESULTS: We found higher time constant over cancerous areas than over healthy tissues. It means that the reaction of affected tissuefis slower after thermal excitation . The temperature recovery to baseline readings takes a longer time over cancerous tissue than in normal, unaffected tissue.

CONCLUSIONS: These unexpected findings of high time constants must be confirmed in a larger sample of breast cancer patients. We also need to establish standard procedures for the imaging sessions so that the results could be repeated as precisely as possible.

KEY WORDS: breast cancer detection, thermal excitation, cold provocation

KÄLTEPROVOKATION VERBESSERT DIE ENTDECKUNG VON BRUSTKREBS MITTELS INFRAROT-THERMOGRAPHIE- EINE PILOTSTUDIE

HINTERGRUND: Frühere Studien zur Brustkrebserkennung mittels Infrarotthermographie haben vielversprechende Ergebnisse geliefert. Wir postulieren, dass die Reaktion auf eine Kälteprovokation an gesunden und karzinomatösen Gewebe unterschiedlich ist. In dieser Studie wurden Kälteprovokation und eine Bewegungskorrektur eingesetzt, um die Ergebnisse zu verbessern.

MATERIALS AND METHODS: Die Krebspatienten stammen aus einer vorläufigen Untersuchung, die im Universitätsspital in Tampere durchgeführt worden war. Drei von neun Patienten waren für diese Pilotstudie geeignet, Wir verwendeten eine ungekühlte mikrobolometrische Infrarot-Kamera IRvox384 , die an der Technischen Universität Lodz für medizischen Anwendungen entwickelt worden waren. Nach 15 Sekunden langer Kühlung wurde eine Serie von 300 Bildern wurde bei Bildrate von 2 Bildern pro Sekunde aufgezeichnet. Die Aufzeichnungsdauer betrug 150 Sekunden.

RESULTS: Höhere Zeitkonstanten wurden über karzinomatösen Gewebe als über gesunden Gewebe gefunden. Das heißt, dass die Reaktion des erkrankten Gewebes auf thermische Reize verlangsamt ist und deshalb die Erreichung der Ausgangstemperatur länger braucht.

SCHLUSSFOLGERUNG: Diese unerwarteten Ergebnisse langer Zeitkonstanten bedarf einer Bestätigung in einer größeren Gruppe von Patientinnen mit Brustkrebs. Außerdem müssen Standards für die Aufzeichnung der Wärmebilder entwickelt und eingehalten werden, um die Ergebnisse mit bestmöglicher Präzision wiederholen zu können.

SCHLÜSSELWÖRTER: Brustkrebserkennung, thermische Reizung, Kälteprovokation

Thermology International 2012, 22(4) 152- 156

Introduction

Breast cancer is the most common cancer among women nowadays [1]. It's very important to diagnose the cancer in an early stage, as e the chance of being cured is 96.3% for tumours less than 2 cm diameter and absent affection of lymph nodes, but the 5 years survival rate decreases to 82,2% in tumours with 2 to 4.9 cm diameter and uninvolved lymph nodes.[2]. Very often early detection is not possible using traditional methods such as mammography, magnetic resonance imaging (MRI) or ultrasonography (USG) [3]. Some of these investigations require ionizing radiation or contrast media and must not be repeated frequently, figure 1.

Screening for breast cancer is primarily based on mammography and secondarily on magnetic resonance imaging (MRI) and medical ultrasonography (USG). The advantage of using mammography is its high specificity is (up to 99,5 %) and disadvantages are that it requires radiation, it is uncomfortable to the patient due to the compression of the breasts, and the fact that the density of the breast tissue affects the sensitivity. MRI has good sensitivity (up to

100 %) and specificity (up to 95 %), but it is expensive, it is time consuming, and requires the application of contrast medium. USG generates a lot of false positive results, but shows good specificity in dense breast tissue. [4]

Due to the non-invasive and, harmless nature of infrared thermography IRT, many trials have been performed to detect and evaluate breast cancer with infrared cameras.A recent study used an artificial intelligence programme to evaluate infrared images for the detection of breast cancer in small sample of 106 women who underwent biopsy with 65 malignant and 41 benign findings. IR resulted in an overall diagnostic sensitivity for breast cancer of 70% and a specificity of 48%., but in small subgroup 21 women under the age of 50 with 9 cancers in total the diagnostic sensitivity increased to 78% and specificity to 75 % [5].

The rationale to detect cancer with IR imaging is based on the fact that metabolic activities of healthy and cancerous tissue differ from each other. Cancer cells exhibit an increased capacity for lactate production as the result of aerobic glycolysis, whilst normal, healthy cells depend on oxidative phosphorylation to synthesize ATP [6]. Very simplified, this results in the fact that tumour cells need mor glucose but less oxygen than healthy subjects. One limiting factor of tumour growth is perfusion, therefore the tumour may stimulate vasculogenesis. The differences in distribution of perfusion are visible in thermography. [1]

Most of the previous studies are based on asymmetric distribution of thermal or texture features (signatures) obtained from infrared images [7-10]. Typically, healthy women have a symmetrical temperature distribution on both breasts, figure 2, [11, 12].

During thermographic measurements it is very important to keep the same environmental conditions. Duration of preparation of subjects being investigated, environmental conditions such as a defined and stable room temperature, body positions during image recording and the field of view of the body part of interest must be standardised. [13-16].

In most cases, the static distribution of temperatures on the breast surface is recorded, and typically cancerous tissue presents with spots of high temperature as shown in figure 3 [17]. Reliable measurements of absolute skin temperature are difficult to perform, because the skin temperature depends on many different factors.

This was the main argument to investigate dynamic changes of temperatures after cooling the skin instead of measuring the absolute tempertures .over cancerous and healthy breast tissue .

Materials And Methods

It is assumed that cancerous tissue has different thermal time constants than unaffected, healthy tissue. The breast cancer had been defined with mammography and/or ultrasound, and biopsy before IR-imaging. The breast cancer was localized from mammography images

The skin of the breast of the patients was cooled for about 15 seconds using a 5mm thick cooling gel pad., which has been stored in a refrigerator for an hour at 4°C. The cooling pad was set directly on the skin covering both breasts, and was removed before IR imaging. Both breasts were cooled to compare the recovery time after cooling.. Measurements were performed for the entire breasts, but motion correction was applied to the selected regions of interest (ROIs.) [18,19]

We measured over time the temperature difference to the baseline temperature recorded immediately after removing the gel, and we plotted recovery curves. Exemplary ima ges from a set of a few hundred recorded for each patient, are presented in figure. 4. A small square region of interest with 16 pixels was defined, fig.ure 3 [20, 21].A sequence of 300 images was recorded at a frame rate of 2 frames per second. The total recording time was 150 s.

The approximation using the exponential function was the next step of the data processing. An example of approximation is presented in figure. 5.

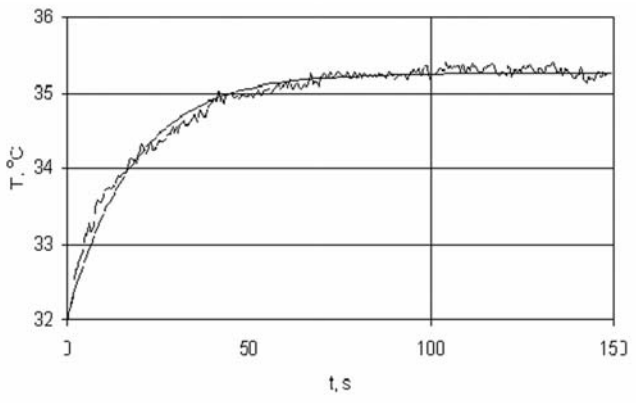

Figure 5.
Approximation of measured temperature recovery curve with exponential function

We assume the single thermal time constant model of the skin. It denotes that the temperature evolution is time can be expressed by the equation (1).

$$T = T_s\left(1 - e^{\frac{\tau}{x}}\right) \quad (1)$$

where Ts is the temperature after full recovery and is the thermal time constant describing the thermal inertia.

The preliminary investigations have been performed as the result of scientific cooperation of Finnish and Polish Technical Universities in Tampere and Lodz. Measurements have been made in Tampere University Hospital using microbolometric uncooled camera IRVox384 thermal camera developed at Technical University of Lodz for medical applications.

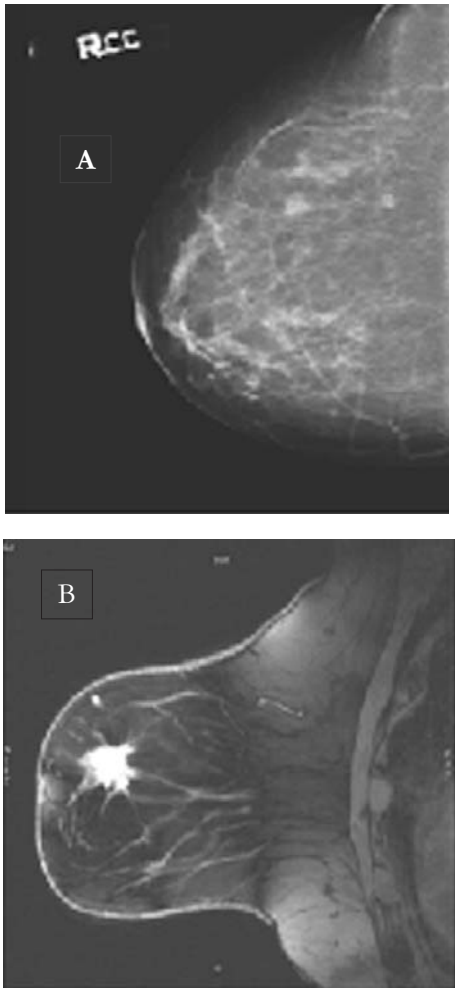

Figure 1
Imaging of breast cancers using mammography (A) and MRI (B)

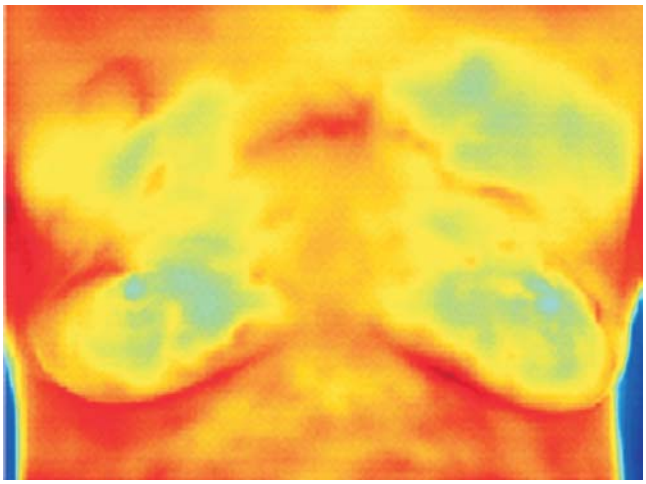

Figure 2
Breast Thermal Image of an healthy woman

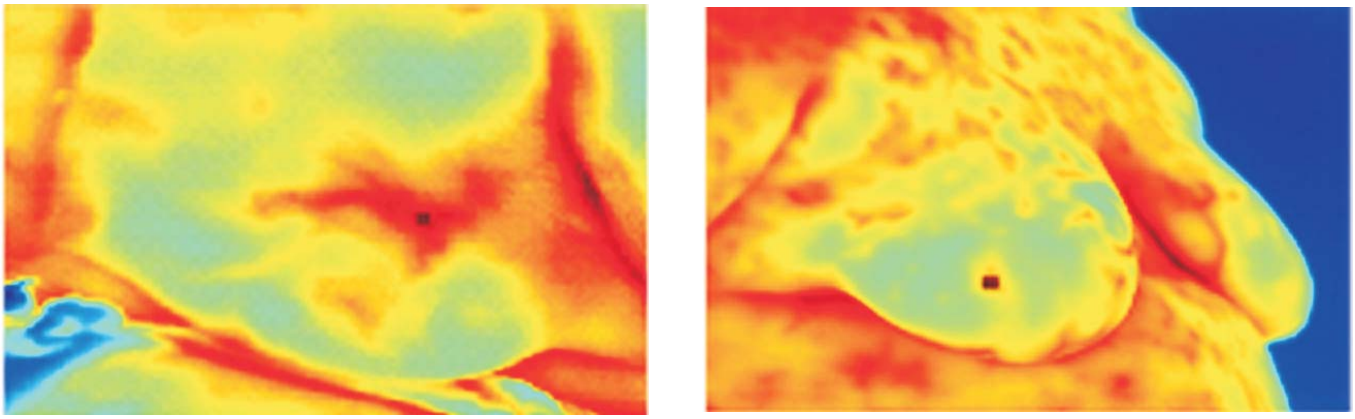

Figure 3.
Breast cancer thermal images, the cancer locatioon position is marked (■)

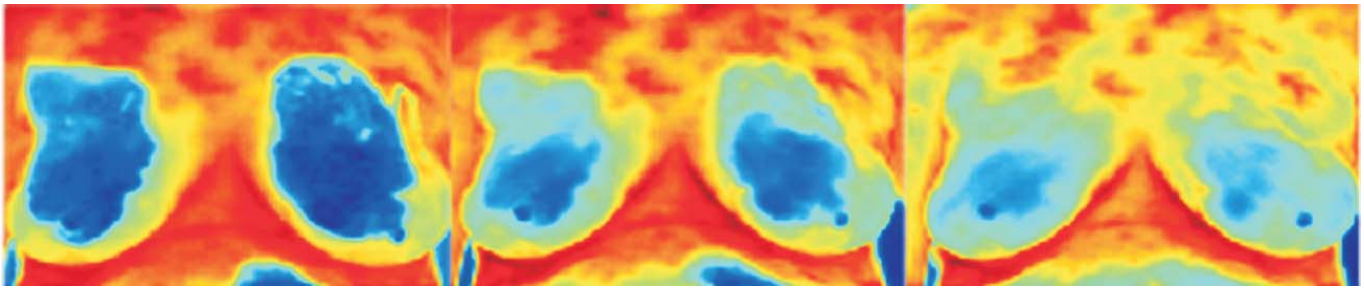

Figure 4.
Breast cancer thermal images, frames no. 1, 32 and 300, sampling rate 0.5 s, total recording time 150 s.

Table 1. Characteristics of the tumors

Patient	Tumor type	Tumor size (pathology)	Grade
B5	Ductal	8 mm	1
B6	Ductal	14 mm	2
B7	Lobular	20 + 10 mm	2

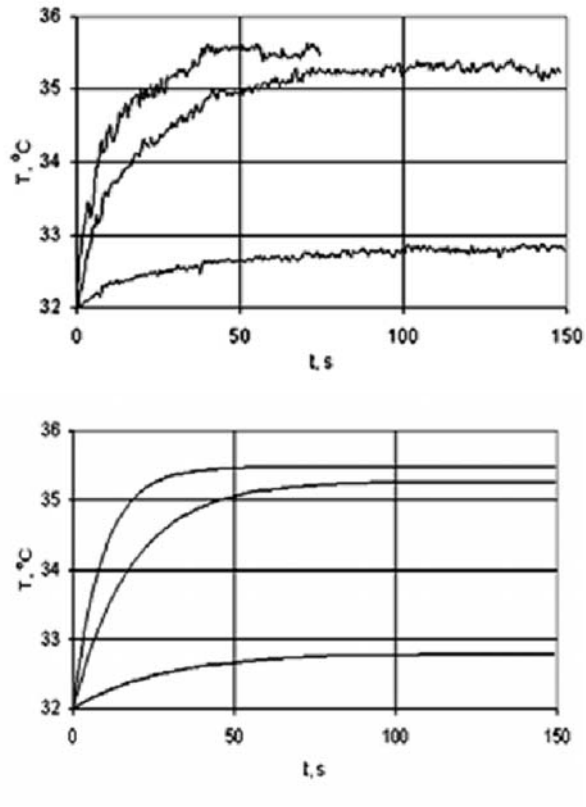

Figure 7.
Temperature evolution for breast cancer tissue after cold

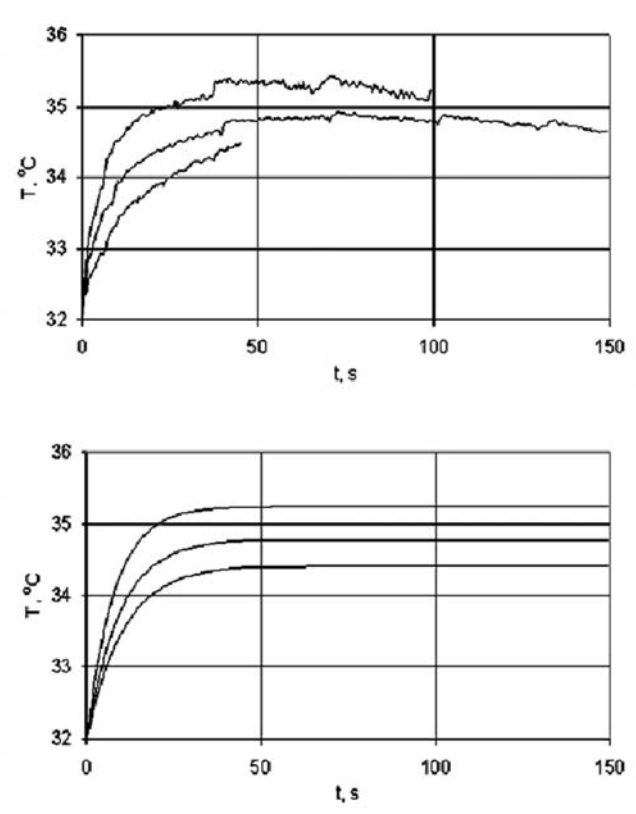

Figure 8.
Temperature evolution for healthy tissue after cold

Table 2.
Single thermal time constant model parameters for 3 cases of breast cancer

Case	Ts, °C	t, s
B5	35,5	9,2
B6	35,3	18,1
B7	32,8	27,5

Table 3.
Single thermal time constant model parameters for 3 cases of healthy tissue

Case	Ts, °C	τ, s
B5	35,2	7,9
B6	34,8	9,4
B7	34,4	10,5

Results

During the investigation 9 cases of breast cancer were examined. Only 3 of them are reported in this work. The main characteristics of the patients' tumours are summarized in table 1 .

The temperature evolution after cold provocation in breast cancer is shown in the diagrams of figure 7. Figure 8 presents the corresponding rewarming curves of healthy tissue. Table 2 lists the parameters of thermal time constants of breast cancer patients, table 3 those constants of healthy tissue.

Discussion

It is obvious, that the value of time constant is higher in cancerous cases. It means that the reaction of unhealthy tissue for thermal excitation is slower. and temperature recovery takes a longer period of time. Infrared radiation from the human skin is closely related to the width of superficial vessels. Dilatation of these vessels leads to higher blood flow, a bigger area for heat dissipation and therefore to higher temperature on the skin surface. However in the current study, the blood vessels induced by tumour growth react to a cold challenge similarly as patients suffering from Raynaud´s phenomenon who are

thermographically characterised by prolonged temperature recovery after cold exposure [22]. This finding is in contrast to the behaviour of other tumours such as malignant melanoma after applying a cold challenge. Di Carlo [23] and recently Santa Cruz et al [24] and Herman & Pirtini Cetingu [25]reported quick recovery of the surface temperature of melanomas after a short period of cooling.

Our preliminary results of rewarming patterns of cancerous breast tissue must be confirmed in a greater sampleof patients with diagnosed cancers. Temperature measurements should be done very precisely taking into account environmental condition andother standard procedures in order torepeat the measurement correctly.

Next step in our investigation is to extract parameters from the thermal model of human tissue which will suit to the experimental results. Then we will be able to do classification for healthy and unhealthy cases in automatic and quantified way.

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(Received on9.8.2012, revision accepted on 4.10..2012)