Infrared Imaging to Measure Cigarette Smoking Induced Vasoconstriction Effects

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ABSTRACT
Scientifically proven adverse health effects of cigarette smoking include increased risks for lung and bronchial cancer and raised LDL (bad) cholesterol blood values. Plus, smoking also increases adrenalin which, in turn, is responsible for vasoconstriction (shrinking of blood vessels), resulting in high blood pressure and restricted blood flow in the extremities, among other health issues. Despite these risks, people are unable to stop smoking for many reasons; nicotine imaging is an excellent means to measure and demonstrate the strong and immediate influences of smoking on the blood supply and heat regulation has a very strong addictive effect, no pain or other immediate biological influences from smoking can be experienced, and life-threatening diseases are typically decades away. Thermal of the extremities. Smokers can convincingly be shown the 'temporary amputation' of their fingertips due to vasoconstriction, even after smoking a single cigarette. Infrared image sequences from a FLIR S60 camera as well as physiological data (heart rate, blood pressure) were acquired from several test subjects in a well-controlled environment before, both during and after smoking for comparison purposes. A task-optimized digital image software package was developed for automatic generation of test results. (The platform-independent executable version of this software will be made available free of charge to anyone interested.) The goal is to increase public awareness to the dangers of smoking and motivate more smokers to participate in programs that help them quit.

INTRODUCTION
Scientifically proven adverse health effects of cigarette smoking include increased risks for lung and bronchial cancer. Furthermore, the increased level of carbon monoxide in the blood due to smoking is responsible for a higher hematocrit value (volume of red blood cells as a percentage of the total blood volume). This together with smoking-induced higher fibrinogen values (a pre-stage of the blood clotting factor fibrin) results in increased blood viscosity and thus a higher risk for e.g. thrombosis, myocardial infarction and stroke. Smoking also increases adrenalin (also called epinephrine), a stimulating hormone which, in turn, is responsible for vasoconstriction (tightening of blood vessels) causing high blood pressure and restricted blood flow to and in the extremities. Moreover, smoking raises LDL (bad) cholesterol blood values and can advance arteriosclerosis which, due to the thickening and hardening of the arterial walls, leads to impaired blood circulation. A special form of arteriosclerosis, the so-called peripheral arterial occlusive disease, often leaves no choice but amputation of an extremity (“smoker’s leg”) to save the patient’s life. Despite all these risks, people are unable to give up smoking. The main reasons might be that nicotine has a very strong addictive effect, that no pain or other immediate biological influences from smoking are experienced, and life-threatening diseases are typically decades away.

Infrared (IR) imaging is an excellent method to measure and demonstrate the strong and immediate influences of smoking on the blood supply and thermoregulation of the extremities: smokers can convincingly be shown the “temporary amputation” of their toes and fingertips due to vasoconstriction, even after smoking a single cigarette. Before we focus on the specifics and design of our small study as well as processing methods necessary for automatic image analysis, we will briefly highlight the importance of medical IR imaging and review the most important facts about smoking and the effects of nicotine in the human body.

MEDICAL INFRARED IMAGING

Infrared (also called thermal) imaging has been increasingly applied in veterinary and human medicine, and active research is ongoing in the medical IR field. The application of imaging modalities, which provide physiological information, and their combination with traditional imaging modalities which provide anatomical information has improved medical diagnoses a great deal (e.g. combined positron emission tomography and computer assisted tomography known as PET-CT imaging). Thermal imaging is capable of delivering physiological, i.e. functional, information with absolutely no risk for the patient. Various inflammations and malignant processes change physiological functions in the body and are often related to increased local body and skin temperatures. Tumor-associated changes in skin surface temperature revealed by infrared imaging have been measured in patients since the early 1960s. Thermal imaging was once employed for breast cancer screening but fell out of favor more than 20 years ago although it was approved by the U.S. Food and Drug Administration (FDA) in 1982 as a supplement to X-ray-based mammography. This failure might be attributed to difficulties in interpreting the thermal images and the use of non-digital imaging devices, rather than the approach being theoretically flawed [1].

Today's state-of-the-art digital infrared imaging cameras can measure skin surface temperatures with high temporal, spatial, and thermal resolutions. In combination with appropriate digital image processing techniques, which can enhance thermal images and extract valuable information, both static and dynamic infrared imaging can be used to precisely and reliably measure changes in human skin temperature. For example, at sites of tumor growth profound vascular changes in the form of angiogenesis (formation of new blood vessels) translate into changes in skin surface temperature. Even very small tumors may produce notable temperature changes due to enhanced perfusion over a substantial area via regional tumor-induced vasodilatation caused by nitric oxide, a molecule with potent vasodilating properties. For these reasons, infrared imaging has great potential as a noninvasive procedure for assessing tumor angiogenesis and for monitoring the activity of antiangiogenic drugs in cancer patients. Thus, a reassessment of infrared imaging as a screening method for breast cancer, particularly in combination with mammography, might be indicated. Furthermore, a new imaging method, called computerized thermal imaging, currently being developed and tested acquires a series of images of the breast and combines the principles of traditional thermal imaging with digital image reconstruction methods to improve breast tumor detection [2].

SMOKING AND NICOTINE

Statistics, types of smoking and some legal aspects

Every day over 15 billion cigarettes are smoked worldwide. According to estimates of the World Health Organization (WHO) there are 1.3 billion smokers in the world — about one-third of the global population aged 15 years and over. Data suggest that approximately 47% of all men and 10% of all women smoke. In developing countries, 58% of men and 9% of women smoke, while in developed countries, 35% of men smoke, as do 22% of women. Tobacco consumption in developing countries is expected to increase as economic development triggers an increase in disposable income.

Besides active smoking, passive ("second-hand") smoking happens when non-smokers are exposed to other people's tobacco smoke. There are two types of cigarette smoke: mainstream and sidestream. Mainstream smoke is inhaled by the smoker through the mouthpiece, which usually contains a filter. Nonsmokers are exposed to mainstream smoke when the smoker exhales. Sidestream smoke is released directly (unfiltered) into the air from the burning end of the cigarette. Many potentially toxic gases are present in higher concentrations in sidestream smoke than in mainstream smoke and nearly 85% of the smoke in a room results from sidestream smoke [3]. While the relative health risks from passive smoking are smaller in comparison to those from active smoking, passive smokers suffer increased risks of many smoking-related diseases in the long term. Almost 50% of all children are exposed to passive smoking at home and parental smoking is known to be a risk factor for lower respiratory tract infections such as bronchitis, pneumonia, bronchiolitis and the sudden infant death syndrome [4].

To reduce the number of smokers, to protect non-smokers from passive smoking, especially at the workplace, and to prevent children from becoming addicted to cigarette smoking might be the main reasons why many countries have introduced laws prohibiting tobacco smoking in public or quasi-public areas (restaurants, bars, hotels, offices, etc.) or even outdoor public areas (parks, sports stadiums)[1].

A directive of the European Union (EU) demands compulsory general warnings to appear on each packet stating that smoking kills or can kill. It is also allowing the introduction of color photographs or other illustrations depicting the health consequences of smoking to accompany the additional warnings on cigarette packets. The shock value of such pictures has proved highly effective in countries such as Canada and Brazil. The directive also bans tobacco advertising in the print media, on radio and on the internet.

Mortality
According to the World Health Report 2002 (WHO) tobacco causes about 8.8% of all deaths (4.9 million per year). Unless current trends are not reversed, this figure is expected to rise to 10 million per year by the early 2030ies, with 70% of deaths in developing countries.

Smoking is a major cause of lung disease (emphysema, chronic bronchitis, asthma, chronic obstructive pulmonary disease), coronary heart disease and stroke. The latter two are strongly linked to arteriosclerosis (clogged and narrowed arteries) which is greatly promoted by smoking. It is important to mention that women aged 35 and over who use birth control pills have a significantly higher risk of heart disease and stroke if they smoke. Risks for other diseases, like cancer of the throat, mouth, esophagus, pancreas, kidney, ureter, bladder, and cervix are also increased by smoking.

Among industrialized countries, the WHO estimates that smoking causes over 90% of lung cancer in men and about 70% in women. In addition, the percentages attributable are 56-80% for chronic respiratory disease and 22% for cardiovascular disease. According to the American Lung Association, smoking is responsible for approximately one in five deaths in the United States, and this number is not significantly different in other countries. From 1995 to 1999, smoking killed over 440,000 people in the United States each year and more than 35 million Americans are now living with chronic lung disease. Excluding adult deaths from exposure to second-hand smoke, adult males and females lost an average of 13.2 and 14.5 years of life respectively due to smoking [5].

Cigarettes
To make cigarettes, the leaves of tobacco plants are first dried and then treated with a variety of chemicals. Many additional ingredients are added for maintaining blend consistency, improving perceived blend quality, and changing the organoleptic qualities of the tobacco smoke. For example, the US government permits the use of about 600 additives in the manufacture of cigarettes. These ingredients are approved as additives for foods but not all have been tested by burning them. Over 4000 chemical compounds are created by burning a cigarette, many of which are toxic, mutagenic or carcinogenic. Carbon monoxide, nitrogen oxides, hydrogen cyanide and ammonia are all present in cigarette smoke. Forty-three known carcinogens are in mainstream smoke, sidestream smoke or both [6]. Tar in cigarettes is the particulate matter, a mixture of substances that when inhaled forms a sticky mass in the lungs on condensation. It is the tar in cigarettes that actually transports many of the dangerous chemicals in cigarette smoke directly into the body. Tar in cigarettes also paralyses the cilia, the small hairs which protect and clean the lungs.

Cigarettes manufactured and sold within the European Union (EU) must not have higher levels than 10 mg of tar, 1 mg of nicotine, and 10 mg of carbon monoxide (CO) while common US cigarettes have about

[1] California was the first state to ban smoking in most bars and casinos in 1998. In New York, smoking has been banned in bars, clubs and restaurants since March 2003. The Republic of Ireland became the first country in the world to ban smoking in all enclosed work places (and hence bars and restaurants) in March 2004. Later, New Zealand (December 2004), Italy (January 2005) and Sweden (June 2005) followed. Australia, Malta, Turkey, Norway, parts of Canada and the US have imposed bans on smoking in bars, clubs, and restaurants. The British government favors a ban for almost all enclosed public areas including offices, factories, cafes, restaurants and most pubs in England within a few years from now. Scotland plans to have a comprehensive ban on smoking in public places in force by spring 2006. Many areas have begun to experiment with outdoor smoking bans in specific areas, especially in public or government-owned spaces. For example, in California, outdoor smoking is banned within 20 feet of all public building entrances, exits, "operable windows," and air intakes. This applies to all public and state-owned buildings. Californian cities such as Davis and Berkeley have banned all outdoor smoking at restaurants and food venues. Selected wards in Tokyo prohibit smoking on the streets and strictly enforce it.

0.5-27 mg tar, 0.05-2 mg nicotine, and 0.5-18 mg CO. According to numbers of the U.S. Federal Trade Commission (FTC), in 2004 approximately 85% of cigarette sales in the U.S. were from light or ultra-light cigarettes (less than 15 mg tar) with the largest market share (43%) falling in the 8-11 mg tar range. To measure the amount of tar, nicotine and CO in cigarettes so-called “smoking machines” are used. These machines "smoke" every brand of cigarettes in the same manner. US companies follow the standardized FTC method, where the machine takes one 2 second-puff of 35 milliliters of smoke each minute.

Although “light” or “ultra-light” cigarettes often have lower tar and nicotine, there is no evidence that these put smokers at lower risks for health problems than the regular ones do [7]. Light cigarettes are designed with tiny pinholes on the filters which dilute cigarette smoke with air. Cigarette makers can also use a faster burning paper wrapped around the tobacco of light cigarettes so that the smoking machines get in fewer puffs before the cigarettes burn down. Both these facts result in less tar and nicotine of light cigarettes when measured by smoking machines. However, many smokers (involuntarily) block the tiny vent holes with their fingers or lips which significantly reduce the diluting effect. To satisfy their nicotine craving, people — as opposed to smoking machines — may inhale more deeply, take longer or more frequent puffs, or smoke extra cigarettes thus maybe inhaling even more tar and nicotine. For these reasons, terms such as "low-tar", "light", "ultra-light" and "mild" as well as new brand names and designs suggesting that a particular tobacco product is less harmful than others, are no longer permitted in the EU.

Nicotine and its effects

Nicotine ($C_{10}H_{14}N_2$) is an organic compound, a naturally occurring alkaloid (like caffeine) and normally constitutes up to about 5 percent of a tobacco plant by dry weight. In small doses nicotine has a stimulating effect, increasing activity, alertness and memory while in repeat users it triggers relaxation but also addiction to e.g. tobacco smoking. In large doses nicotine may cause vomiting, nausea, headaches, difficulty in breathing, stomach pains, diarrhea, dizziness and seizures. Nicotine is a potent nerve poison and is included in many commercially sold insecticides. The lethal dose LD50 which causes the death of 50% of a group of test animals is about 50 mg per kg of body mass for rats and 3 mg/kg for mice. 40-60 mg (0.6-1.0 mg/kg) can be a lethal dosage for adult human beings, i.e. the quantity contained in approximately 2 grams of tobacco. This would be the amount contained by only a few common blend cigarettes if all of the nicotine was absorbed, e.g. by ingestion. However, death from nicotine overdose is not common because gastric emptying and the neutralizing effect of the stomach's acid delay the gastric absorption of nicotine. As a consequence, vomiting caused by the initially absorbed fraction generally removes much of the tobacco from the stomach.

Nicotine has an effective half-life of about 2 hours, meaning that twelve hours after smoking a cigarette only about 0.0156 milligram per 1 milligram of absorbed nicotine remains in the body. The metabolism of nicotine occurs mainly in the liver with the production of cotinine and nicotine-N-oxide, which are then excreted in urine. Nicotine is also excreted in the milk of nursing mothers who smoke.

Nicotine from chewing tobacco and snuff is absorbed through the oral and/or nasal mucosa. The most common and the most expedient way to get nicotine into the bloodstream is through inhalation, i.e. by smoking it. The lungs are lined with several hundred million alveoli, the tiny air sacs with an average diameter of about 200-300 microns, where the pulmonary gas exchange occurs. These alveoli have an enormous surface area of about 60-100 m^2, and thus provide ample access for nicotine and other compounds to enter the blood in the pulmonary capillaries. Nicotine then quickly becomes distributed in the body through the venous circulation and systemic arterial bloodstream, and needs on average about 10-19 seconds to cross the blood-brain barrier and reach the brain. Following cigarette smoking, the arterial blood perfusing the brain contains levels of nicotine which exceed venous levels by a factor of two to six [8, 9].

Cardiovascular effects of nicotine

Nicotine effects on the cardiovascular system are mediated by sympathetic (autonomic) neural stimulation. Nicotine causes sympathetic stimulation through central and peripheral mechanisms. Central nervous system-mediated mechanisms include activation of peripheral chemoreceptors, particularly the carotid chemoreceptor, and direct effects on the brain stem and spinal cord. Peripheral mechanisms include release of catecholamine from the adrenal glands and vascular nerve endings leading to an increased flow of adrenaline The rapid release of adrenaline causes an increase in heart rate and blood pressure when nicotine is delivered via cigarette smoking, chewing gum, nasal spray or intravenous infusion [10,11,12].

Nicotine affects blood flow to different organs, causing vasoconstriction in coronary arteries and the vascular beds of the skin [13]. Since blood not only circulates oxygen and nutrients but also internally generated heat to the extremities, one of the consequences of lowering blood flow is the cooling of the extremities. Cutaneous vasoconstriction decreases capillary blood flow and results e.g. in a significant decrease in fingertip temperature [10]. Nicotine also affects hemostasis by increasing thrombogenesis and platelet aggregation. In the long term, nicotine can increase levels of "bad" cholesterol (LDL) which damages arteries and increases the risk for a heart attack or stroke.

Effects of nicotine on the brain
Another effect of nicotine is that it stimulates the brain to produce more endorphins. Endorphins are small proteins that are often called the body's natural pain killer. Their chemical structure is very similar to that of heavy-duty synthetic painkillers like morphine. Endorphins can lead to the feeling of euphoria that e.g. kicks in during a rigorous race, giving the runner a mental edge to finish the race while temporarily masking the nagging pains he or she might otherwise feel.

In addition, smoking tobacco inhibits monoamine oxidase (MAO) in the brain, an enzyme responsible for breaking down monoaminergic neurotransmitters such as dopamine. Smoking increases dopamine levels in the brain regions that control pleasure and motivation thus actually generating feelings of pleasure and arousal which create a dependency cycle demanding cyclical satisfaction. This reaction is similar to that caused by other abused drugs such as amphetamine, alcohol, cocaine and heroin. A typical smoker takes about 10 puffs of a cigarette over a period of 5 minutes. Thus, a person who smokes about 1 pack (20 cigarettes) daily, gets 200 "hits" of nicotine each day to sustain high dopamine levels. The rapid delivery of nicotine to the brain also allows the smoker to manipulate and adjust the dose of nicotine from a cigarette to achieve a desired effect. All these factors contribute considerably to nicotine's highly addictive nature. The dependence produced by cigarette smoking is very persistent: although around 80% of smokers express a desire to quit the habit, only about 35% attempt to stop each year, and fewer than 10% are successful [14]. While there are many casual users of alcohol, very few individuals smoke tobacco in small enough quantities to avoid dependence.

Quitting smoking and nicotine replacement therapy
Giving up smoking is harder for some smokers than for others. It is generally the case that quitting is more difficult for those who smoke more cigarettes or have smoked longer. Smoking cigarettes is addictive in two ways — physically and psychologically. After stopping smoking a person may experience withdrawal symptoms from the addictive drug nicotine. Psychologically, one needs to break the strongly ingrained habit of smoking. To quit successfully, both physical and psychological factors need to be addressed.
Medicines can double the chances of quitting, i.e. from 10% to 20% success rate after 12 months. There are two types of pharmaceutical products that can help reduce withdrawal symptoms: 1. nicotine replacement therapy (NRT) and 2. buproprion. Some doctors also recommend the use of a specific antidepressant medication to assist in smoking cessation although antidepressants themselves can have serious side effects. There are also several unconventional approaches to quit smoking, e.g. hypnosis and acupuncture.

1. *Nicotine replacement therapy* involves "replacing" the nicotine in a cigarette with another form and helps relieve some of the withdrawal symptoms people experience when they quit smoking (nicotine cravings, insomnia, fatigue, inability to concentrate, headache, cough, sore throat, constipation, stomach pain, dry mouth, sore tongue and/or gums, postnasal drip, depressed mood, etc.). Types of therapy include patches, gums, lozenges, tablets, inhalers, and nasal spray. Nicotine replacement is intended to be used for about three months, which allows the former smoker to focus on the psychological aspects of quitting. Because nicotine is an addictive substance there is a risk of becoming dependent on the nicotine replacement products, but this risk is known to be small compared to the risks of continuing to smoke.

2. *Bupropion* is a prescription-only medicine that does not contain nicotine and was originally intended as an antidepressant. Its ability to help people quit smoking was discovered when participants in early clinical trials lost their desire to smoke. Currently, the actual mechanisms behind bupropion's action are not known. As it is a relatively new drug, there is less experience with it than with NRT. Like all medicines, it has side effects, which may put people off using it. There are also some people who are not suitable for this type of medicine.

Current products can neither mimic the extremely high and rapidly acquired arterial nicotine concentrations (sharp-spike delivery) which occur when tobacco products are inhaled, nor the associated rapid pharmacological effect. This is the main reason, along with the much lower nicotine levels compared to cigarette smoking, why smokers are not completely satisfied with current pharmaceutical products.

One of the largest fears of smokers, especially women, is to gain weight after quitting smoking. Nicotine may increase the basal metabolic rate with concomitant appetite suppression, thus smokers weigh on average less than non-smokers [15]. Nicotine may suppress insulin output from the pancreas which regulates the uptake of excess glucose from the blood. This means that nicotine makes people somewhat hyperglycemic (having more sugar than usual in their blood) and could be one explanation for appetite suppression: due to the increased level of blood sugar, hormones and other signals that are perceived as hunger may be down-regulated. Quitting cigarette smoking is associated with an increase in appetite and caloric intake, with a subsequent weight gain over 6-12 months. Thereafter, both caloric intake and weight return to baseline [16].
It should also be mentioned that often one type of oral gratification or self-soothing (smoking) is substituted with another (eating). Psychological support to strengthen self esteem as well as diet and exercise play important roles in quitting smoking if weight gain is of major consideration.

One main reason for this paper is to provide additional evidence for the strong and immediate impact of smoking on the body in the form of thermal images and temperature curves demonstrating vasoconstriction. This might motivate more smokers to quit smoking and lead to a reduction of the relapse rates.

MATERIALS AND METHODS

Set-Up

To rule out physiological influences from ambient temperature variations, all experiments were performed in a temperature-controlled room. The room temperature was in the range (24.4 ± 0.3)°C, low enough to avoid passive sweating. Relative humidity lay between 49% and 51%. Room temperature and humidity were monitored over the entire course of the experiments (~4 hours) using a digital thermo-hygrometer (CEM DT-321).
The volunteers sat in a comfortable chair approximately 0.3 meters in front of a wall with constant temperature. 0.15 meters from the wall a wooden frame (width 1.3 m x height 1 m) covered with black felt (emission coefficient ε=0.97) hung down from the ceiling and served as a "background", representing room temperature. The IR camera was positioned 1 meter away from the felt material and focused on the subjects' hands. With this recording geometry, optical magnification and image focus depend strongly on axial distance between camera and object. Therefore, a 20-mm-diameter heat insulating spacer protruding from the felt by about 0.1 meters was used to guarantee constant camera-to-object distance. To facilitate correct positioning, the volunteers were able to watch thermal images of their hands live on a TV set. To avoid psychological influences, a black and white binary palette was chosen for display and no temperature scale was visible on screen.

Infrared Camera

We used a FLIR ThermaCAM S60 infrared camera with its standard optics (24° x 18°, angular resolution 1.3 mrad). In our set-up the horizontal and vertical fields of view (FOV) corresponded to approximately 0.41 m and 0.32 m, respectively. Each of the 320x240 detector pixels thus covers an object area of 1.3 x 1.3 mm, the practical instantaneous FOV (IFOV, spot size) is about 3.9 x 3.9 mm. The S60 was placed on a tripod and switched on 150 minutes before the experiments started in order to approach thermal equilibrium. To achieve the best pixel uniformity of the microbolometer array and avoid temporal drifts as much as possible, internal camera calibrations were carried out automatically 30 seconds before every image acquisition. This was managed by using a software tool provided by FLIR Sweden. Since high frame rates are not necessary in our application, temporal image averaging was used to reduce thermal noise.

Subjects
The subjects were 15 adult volunteers, 12 males and 3 females (age range 19-38 years, height range 1.62-1.87 m, weight range 54-105 kg), all students or employees at the Division of Medical Information Technology at the Carinthia Tech Institute, Austria. Eleven volunteers had been smoking 7-30 cigarettes per day for 2-15 years. Four had had been non-smokers for at least 2 years but agreed to inhale the cigarette smoke for the experiment. All subjects rated — on a scale from 1 to 5 with 1 being the best — their own state of health (mean 1.7, standard deviation, SD=0.6) and physical constitution (mean 2.9, SD=1.2). They received no compensation, signed written consent forms, and were informed that termination of participation was possible at any time without penalty. The emission coefficient of the skin was set to 0.98 for all subjects [17].

Cigarettes
All volunteers smoked normal-size filter cigarettes from the same freshly opened packet. The cigarette brand chosen had the following values printed on the packet: nicotine 0.7 mg, tar 8 mg, carbon monoxide 9 mg.

Experimental Protocols
The volunteers were asked not use hand creams on the day of the experiment and not to drink coffee, tea, energy drinks or coke and not to smoke cigarettes 2 hours prior to data acquisition. 30 minutes before the start of the experiment, hand-washing and holding of (cold) beverages was not permitted. Upon entering the temperature-controlled room the subjects were asked to sit down and put a heart rate detection strap around the chest. After 10 minutes of acclimation the experiment was started by measuring blood oxygenation level (Palco 340), blood pressure (Omron F3) and heart rate (Suunto X6 HR). Each of the subjects then lit a cigarette and started smoking as they normally would, holding the cigarette with the left hand only. Thermal images of the subjects' right hand were acquired every minute for 15 minutes. Heart rate and blood oxygen levels were measured at 30 s intervals. At the end of the experiment blood pressure was again measured before each subject immersed the right hand for 30 s into a 40°C distilled water bath. A thermal image was taken after careful hand-drying to provide a reference for image processing. Only for a few seconds of each image acquisition did the subjects have to position their right arms and hands approximately parallel to the floor and perpendicular to the camera's fixed viewing direction while the backs of their hands made contact with the spacer to guarantee constant axial distance from the camera. The subjects were told to spread their fingers during this time. The TV set made correct positioning easy. For reasons of comparison, the experiment was also performed with a few of the volunteers following the same experimental protocols but without cigarette smoking.

Image Processing
The task of image processing is to analyze the acquired thermal image sequences and calculate temperatures as a function of time. By using commercial software programs it is easy to determine the average temperature within a manually selected region of interest (ROI) inside the target (palm, fingers, etc.) in a single image. However, this simple method is only successful when the exact same target area can be selected in all images of the sequence. Furthermore, typical ROIs that can be chosen are rectangular or circular and do not generally match the target's shape. Some programs allow the selection of polygons but this process is tedious and still only approximates the target's shape. In all these cases, the ROI must be chosen smaller than the target because background pixels must not contribute to the calculated mean temperature inside the target, consequently leading to a loss of information. Furthermore, the manual selection of appropriate ROIs can be problematic for small targets such as fingers or fingertips.

For accurate temperature calculations, two tasks need to be carried out by image processing: 1. finding the same target area in all images of a sequence, uninfluenced by target displacements and rotations (detection and alignment); and 2 separating target and background in this area (segmentation). To make automatic analysis easier, we chose a set-up that prevented defocused images and optical magnification changes although the targets were placed close to the IR camera lens (see subsection “Set-Up”). This is important since then the target area (e.g. a subject’s hand) is the same in all images without the need for image scaling.

1. *Target detection and alignment:* It is not desirable in practice to unnaturally fix the position of a subject’s hand over a time period of 15 minutes. Thus, the successive re-positioning of the hand for image acquisition at 1 minute intervals results in relative displacements and rotations from image to image. Automatic detection and alignment works best when the targets in consecutive images have high similarity. However, especially the temperatures of fingers and fingertips can change rather dramatically when smoking a cigarette which results in quite pronounced target decorrelation. Thus, it is necessary to add morphological information in the form of geometrical shapes to facilitate target alignment (also called “registration”). This is one of the reasons why, in this study, the subjects were told to spread their fingers when thermal images were acquired. Furthermore, our intention was to separately display the temperature of the palm and fingers to increase diagnostic information. It is clear, however, that the spreading of the fingers cannot be consecutively performed in exactly the same manner. A certain amount of decorrelation is thus present in practice when the task is to detect and register a subject’s hand.

For target detection and image registration we used an extended two-dimensional (2-D) crosscorrelation-based image registration technique [18]. Crosscorrelation is a method used to optimally detect signals in white Gaussian noise and is quite robust with respect to various image distortions commonly present (see Fig. 1) [19]. However, crosscorrelation-based techniques are vulnerable to target rotations. This is why we extended the conventional crosscorrelation approach by a computationally efficient multi-resolution technique with nearest neighborhood interpolation to achieve robustness in terms of target rotations (Fig. 2). Overall, the extended 2-D crosscorrelation-based procedure allows the automatic detection of a user-selected rectangular ROI in all images of the sequence by correcting for lateral displacements and rotations, and thus provides spatially registered images that make further image processing easier.

2. *Image segmentation:* Several methods are available to automatically distinguish between the object(s) of interest and the “rest” (background) and to assign image pixels to either target (palm, fingers, etc.) or background. This process is known as “image segmentation”. Image segmentation relies on the fact that some kind of “difference” between target and image background exists (e.g. in gray level, temperature, color, texture, etc.). In standard situations, a histogram-based global thresholding technique optimal in terms of minimum separation error [20] shows excellent performance (see Fig. 3, left). However, for the task at hand, proper image segmentation is more challenging since the temperatures of fingers and fingertips can be as low as room (background) temperature, leaving no criterion for segmentation. We found that when people smoke, their fingertips can appear even colder than the background on thermal images (see Fig. 3, right, and section “Results”). Heating or cooling of the background area should not be performed since this might influence the heat regulation of the volunteer sitting right in front of the background. Although infrared markers attached to the subjects’ hands or fingers would make image processing easier, we decided not to use these in order to avoid any interference with a subject’s skin and keep subject preparation as simple as possible.

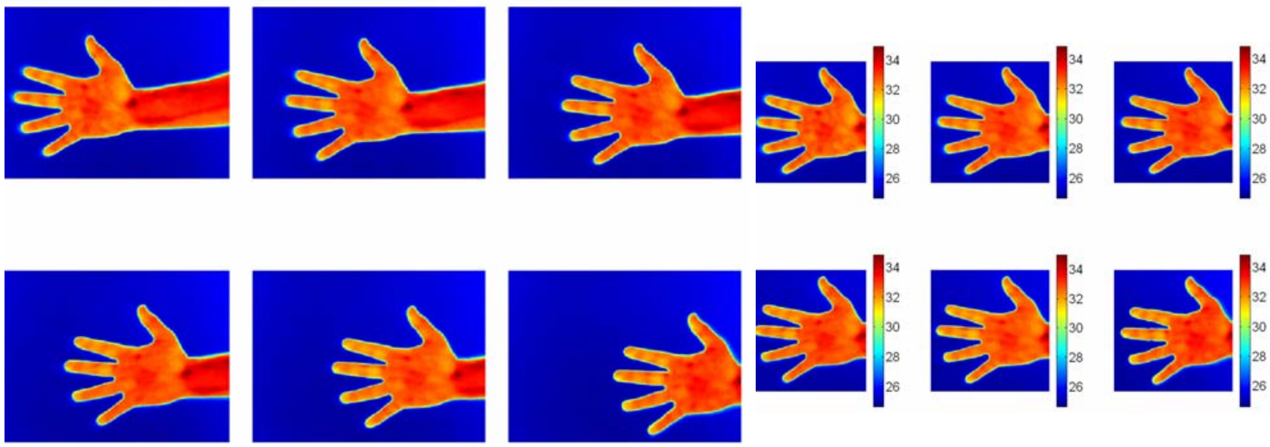

Figure 1. Left: Test sequence of six thermal images (233x306 pixels) of a volunteer's lower arm and hand with horizontal displacements much larger than to be expected in our set-up. Right: Successful detection of a user-selected ROI (188x178 pixels) in all images on the left results in the registered image sequence shown.

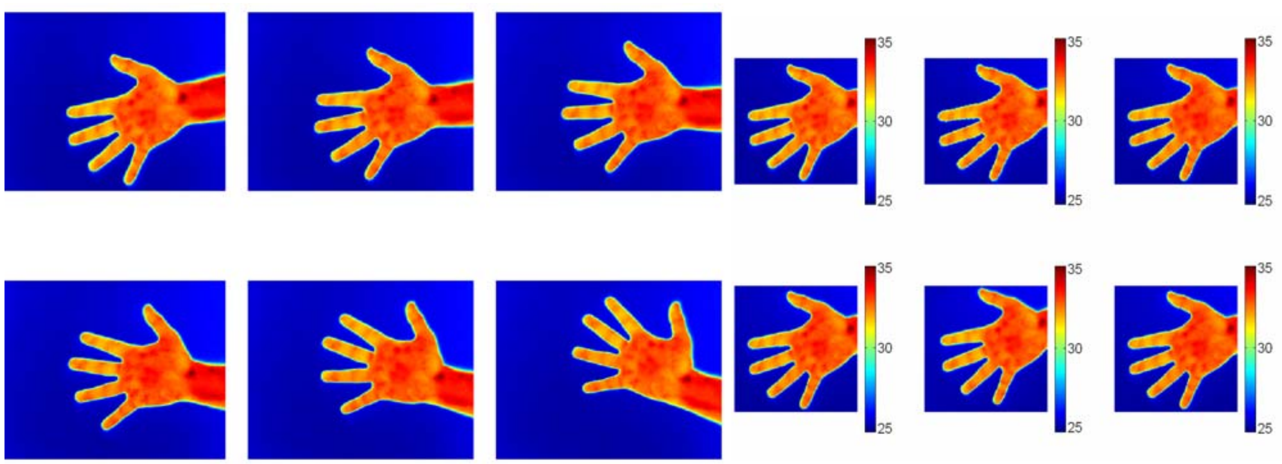

Figure 2. Left: Test sequence of six thermal images (236x303 pixels) of a volunteer's lower arm and hand with rotations much larger than to be expected in our set-up. Right: Successful detection of a user-selected ROI (188x186 pixels) in all images on the left and correction of rotation results in the registered image sequence shown.

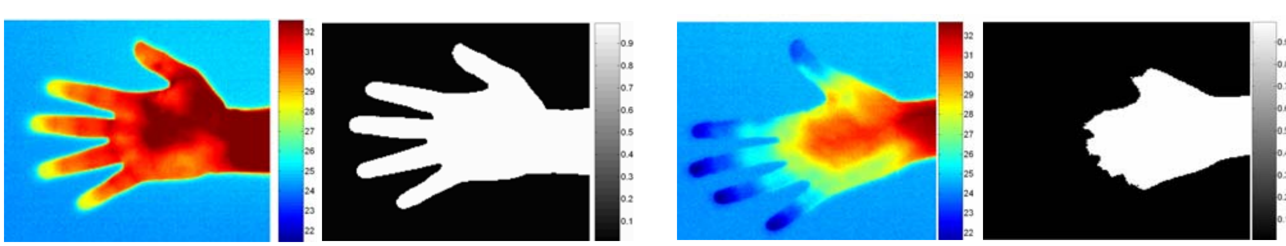

Figure 3. Left: Thermal image of a volunteer's hand before smoking, and binary image where all image pixels that belong to the hand (target) were easily found by a global thresholding technique and assigned the value 1 (white). This binary image can be used as a mask to be multiplied with the original thermogram to extract all pixels inside the hand. Right: Thermal image of another volunteer's hand after smoking a cigarette with fingertips colder than the background, and binary mask where the same thresholding technique falsely assigned a significant number of target pixels the value 0 (background, black).

One way to overcome the segmentation problem illustrated in Fig. 3, right, is to apply two global thresholds which can be determined using the histogram (Fig. 4, left). The histogram shows the number of pixels that lie within certain temperature ranges and has a peak at background temperature level for all thermal images in our study. The width of this peak depends on the levels of statistical thermal noise and fixed pattern noise (IR detector array and/or background non-uniformity). The two thresholds were chosen symmetrically about the histogram peak level with a temperature span of ±2% of the peak level. Figure 4, right, shows that some pixels inside the fingers are not assigned to the target. Note, however, that the temperature range in which these missing finger pixels lie is known, i.e. between the lower and upper threshold levels. Once fingers and palm have been separated from the background and the number of missing pixels is determined, the mean temperature of the fingers can be calculated as will be explained in the following paragraph.

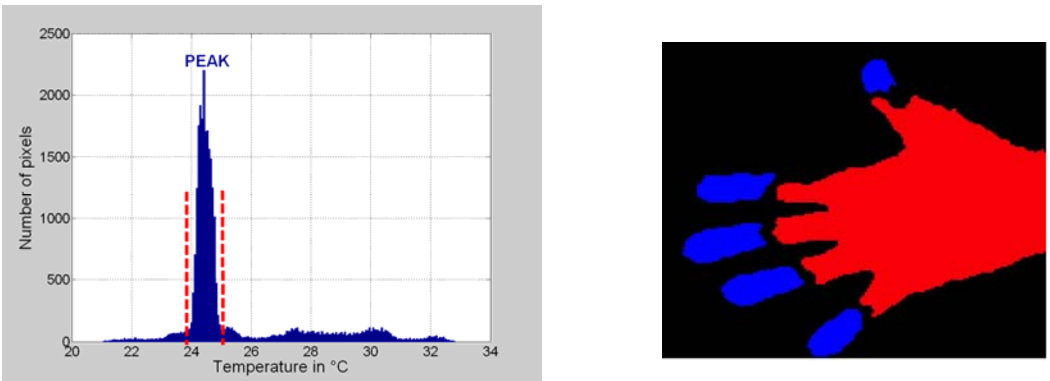

Figure 4. Left: Histogram of the thermal image depicted in Fig. 3 (right) also showing the lower and upper threshold levels (broken vertical lines) used for double thresholding. Right: Resulting binary mask that includes target pixels with both temperatures higher than the upper threshold level (red region) and lower than the lower threshold level (blue region).

To separate palm and fingers, adaptive binary morphological image processing can be applied. In particular, morphological opening with an appropriate structuring element (SE) to eliminate the fingers and thumb was used on the properly segmented reference images acquired from every test person. It is important to first perform the morphological processing with thermal reference images where the subjects immersed their hands into a warm water bath. Optimal segmentation into hand and background is easy to achieve in this situation because all hand regions (even the fingertips) have higher temperatures than the background (similar to Fig. 3, left). The circular-shaped SE was automatically found by iteratively increasing its diameter and calculating the circumference C of the structure that remains in the binary image after morphological opening. When C rapidly decreases, the diameter of the SE has become large enough to successfully eliminate the fingers and thumb in the image (see Fig. 5, left). This SE diameter is then increased by 50% for morphological reasons to finally generate the binary image mask depicted in Fig. 5, middle, where only palm pixels remain. The binary complements of this mask, with regard to the entire hand, represent the fingers and thumb and are used to calculate their entire area as a reference point (see Fig. 5, right). If one wishes to exclude all pixels of the thumb, an additional processing operation is necessary (not shown).

Once the appropriate SE has been determined for each person's hand using the reference images, it can be applied to all thermal images taken from this person to finally extract the palm simply by multiplying the binary masks with the corresponding thermal images. All other (non-palm) pixels of the thermal image are then analyzed using the double threshold technique described above to distinguish between fingers and background. When finger and background temperatures are very similar, even double thresholding misses some finger pixels. However, the mean finger temperature T_{Mean} can be calculated quite accurately by using:

$$T_{Mean} = \frac{N - N_1}{N} \cdot T_{Background} + \frac{N_1}{N} \cdot T_{Fingers}.$$

$T_{Fingers}$ is the mean temperature of the N_1 finger pixels found by double thresholding. The mean background temperature $T_{Background}$ is calculated in a rectangular ROI defined by the maximal and minimal coordinates of the N_1 finger pixels. N, is the number of all finger pixels representing the total finger area, is known from each person's reference image and is constant for all images acquired from this person.

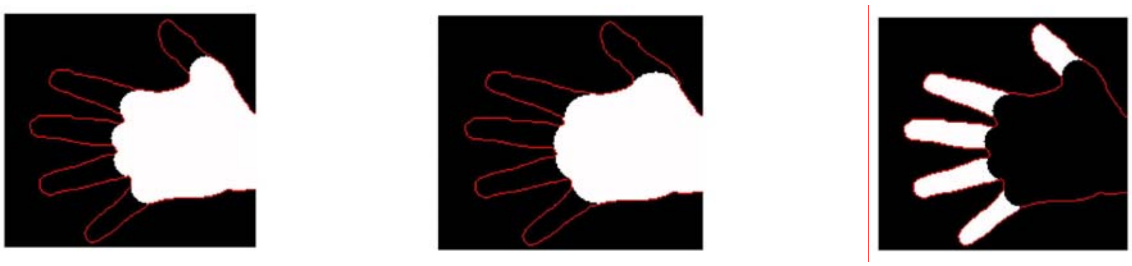

Figure 5. Left: Result of morphological opening with a structuring element (SE) large enough to eliminate the fingers and the thumb. Middle: Application of a 50% larger SE gives the depicted binary mask (white) used to extract the palm. Right: Binary complement of the mask in the middle with regard to all pixels inside the hand which only comprises finger and thumb pixels. The red line representing the hand contour was added for demonstration purposes only.

RESULTS

First, we evaluated the thermal image sequences acquired from two subjects (one smoker, one non-smoker) when no cigarettes were smoked. Then the image sequences from all 15 cigarette-smoking subjects were analyzed. We applied the image processing procedures described in the "Methods and Materials" section to automatically generate plots showing the temperatures of the palm and the fingers of each subject over time as well as the background (room) temperature. (The latter was calculated from the thermal images with high precision by averaging a large number of background pixels). Monitoring the room temperature is important since any changes in skin temperature cannot be attributed to the room temperature if this remains constant. To take into consideration that the temperatures within the palm and fingers are spatially inhomogeneous, we calculated maximum, mean (plus standard deviations, SD) and minimum temperatures as functions of time.

The experimental results when no smoking took place are as expected: palm, finger and background temperatures are constant over time (not shown) which confirms that our set-up and environment were appropriately chosen. When the subjects smoked, the hand and palm temperatures changed significantly over time. Figure 6 representatively illustrates the temperature development of a habitual smoker's hand at 2-minute intervals. The hypothermic effect is most pronounced in the fingertips.

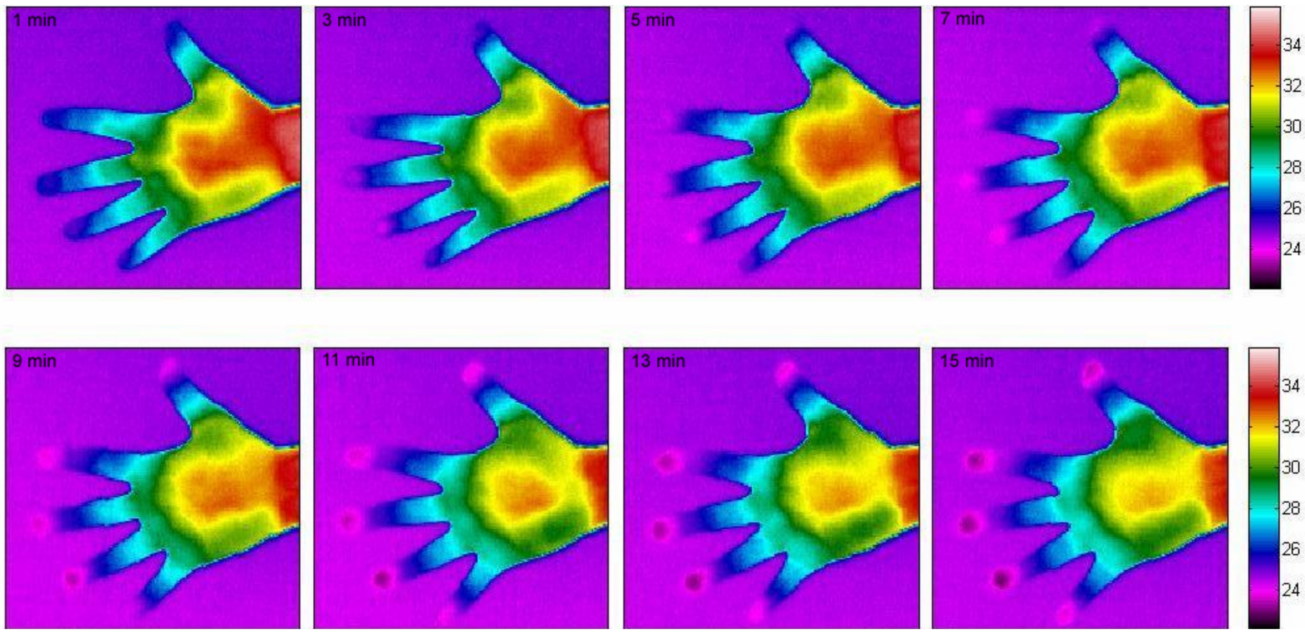

Figure 6. Registered thermal image sequence of a habitual (female) smoker shown at 2-minute intervals, starting 1 minute after smoking commenced. All images are displayed at the same level and span. This person smoked the cigarette down to the stub in 4.5 minutes. At the beginning, finger tips were warmer and at the end even colder than background (=room) temperature. This unexpected behavior was double-checked using a digital thermometer for verification..

Figure 7 depicts the temperature development of the habitual smoker's hand shown in Fig. 6 which we found to be typical in smokers when the experiment was performed during smoking. In this person, the temperatures drop significantly over 15 minutes (e.g. mean temperatures: palm -1.2°C, fingers –1.8°C).

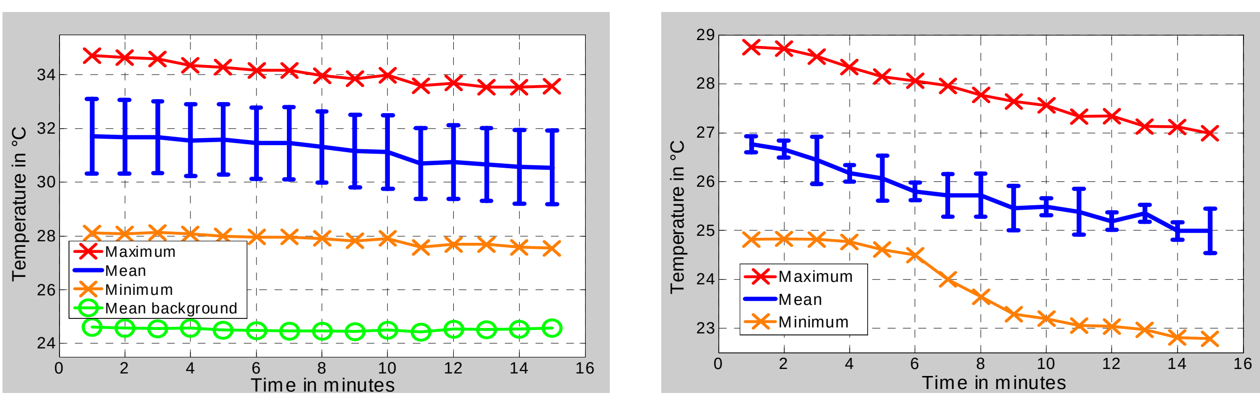

Figure 7. Left: Palm temperatures of the habitual (female) smoker's right hand shown in Fig. 6 over time when smoking took place. The background temperature was highly stable with a 15-minute temporal mean value of 24.52°C (SD 0.053°C). Right: Corresponding finger temperatures. All error bars indicate ± 1 standard deviation (SD).

Figure 8 illustrates the average temperature curves calculated from the mean palm and finger temperatures of 9 smokers when smoking took place. Two smokers had to be excluded due to inappropriate image quality. Over 15 minutes the mean temperatures of the subjects' palm and fingers decreased on average by about 1°C and 1.5°C, respectively.

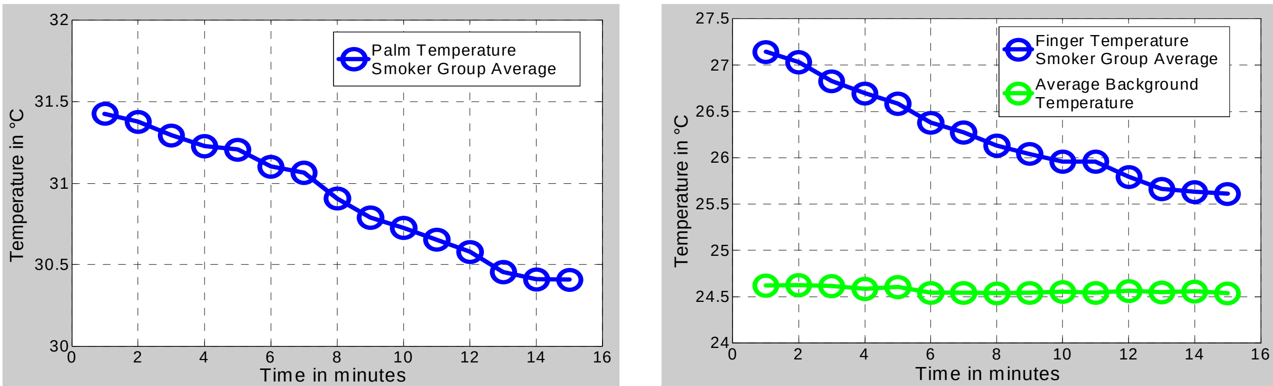

Figure 8. Left: Average of the mean palm temperatures of 9 smokers when smoking took place. Right: Corresponding finger and background temperatures. The 15-minute temporal mean value of the latter is 24.57°C (SD 0.033°C).

Figure 9 shows the temperatures of a non-smoker's hand over time during smoking. Including non-smokers in our study was originally intended only for control purposes, which is why available data are limited to 4 subjects. During data analysis it turned out that the palm and finger temperatures of non-smokers actually increased when smoking took place (see Fig. 9). This behavior was found in all 4 non-smokers which was not to be expected. Nicotine and adrenaline are known to affect blood flow to the various organs differently, causing vasoconstriction in smooth muscle and the vascular beds of the skin, and vasodilatation (widening of blood vessels) in others, e.g. heart and skeletal muscles [10]. Additionally, the effects of nicotine are characterized by the fact that after initially stimulating its receptors, nicotine subsequently desensitizes them, which might be of relevance for our findings. Moreover, many blood vessels have nonadrenergic noncholinergic innervation and these nerves contribute to vascular tone control although peripheral blood vessels are mainly regulated by vascular adrenergic nerves.

At this time it is not clear why the vascular bed of human skin behaves differently for smokers and non-smokers when smoking takes place. Further investigations into the causes and with a larger number of non-smoking subjects should to be performed for more accurate results.

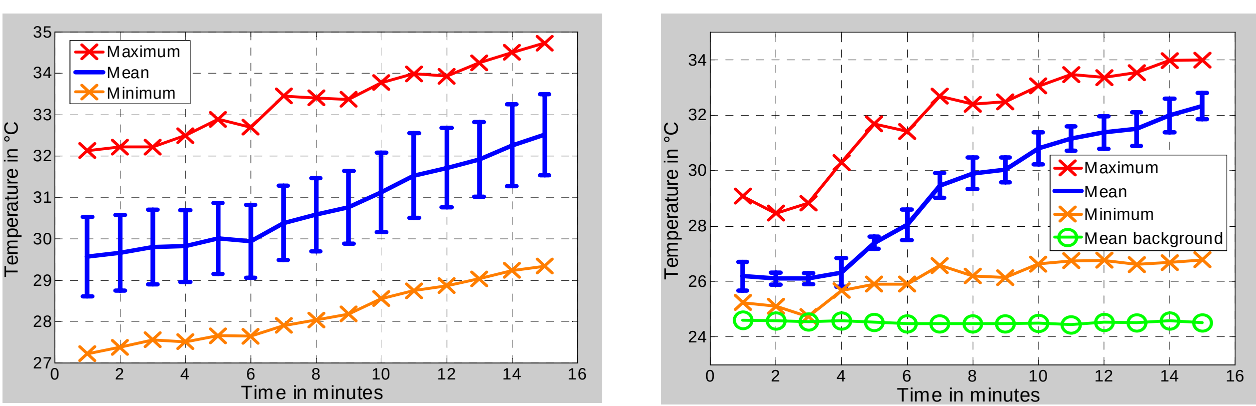

Figure 9. Left: Palm temperature development of the non-smoker who showed the highest temperature increases when smoking took place. The mean palm temperature increased by almost 3°C. Right: Corresponding finger temperatures where even higher temperature increases were found. The background temperature was again virtually constant.

Finally, table 1 depicts the average values of the heart rate and blood pressure at the beginning of the experiment before smoking, and after 15 minutes at the end of the experiment. Heart rates are also shown 5 minutes after the test persons started smoking. It took the subjects 5.9 minutes on average (SD 1.1 minutes) to smoke the cigarettes down to the filter. Blood oxygenation values measured with our pulseoximeter are not shown, since no significant changes from base level (~ 98%) occurred.

	SMOKERS		NON-SMOKERS	
Time in minutes	**Heart rate** in beats per minute	**Blood pressure** in mmHg	**Heart rate** in beats per minute	**Blood pressure** in mmHg
0	80.5	121 / 71	67.8	138 / 84
5	88.0	-	65.3	-
15	80.9	125 / 74	61.3	131 / 79

Table 1. Average values of the heart rate and blood pressure (systolic/diastolic). Measured values were averaged from 11 subjects in the smoker group and from 4 subjects in the non-smoker group, respectively.

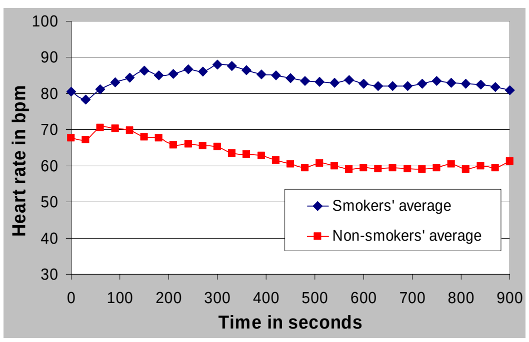

Figure 10. Average values of the heart rate over time. Values were measured at 30-second intervals from all 15 subjects and averaged from 11 subjects in the smoker group and from 4 subjects in the non-smoker group, respectively.

The data in table 1 and Fig. 10 support our results from IR imaging that smoking-induced (cardio)vascular effects in non-smokers are opposite to those in habitual smokers: heart rate and (here with lower significance) blood pressure in all 4 non-smokers participating in this study decreased when the subjects smoked a cigarette. Decreases in blood pressure correlate with the vasodilation detected by thermal imaging.

It is known that smokers develop a rapid tolerance to nicotine with regard to increased heart rate [10]. The first cigarette of the day produces significantly greater increases in heart rate than subsequent cigarettes. This realization, coupled with the fact that our experiments were carried out in the afternoon, correlates well with the average heart rate of the smoker group shown in Fig.10.

SUMMARY

Infrared imaging has many applications in medicine and is, in particular, a sensitive and reliable method to determine human skin temperatures. We measured the temperature development of the palm and fingers and also acquired physiological data of 15 human subjects before, during and after cigarette smoking to demonstrate smoking-induced vasoconstriction. To automatically calculate temperatures over time, appropriate digital image processing methods for target detection and registration as well as image segmentation and discrimination of palm and fingers were implemented. Results found in the smoker group (11 subjects) are in agreement with the known facts of significant skin temperature decreases in the extremities, and increases in heart rate and blood pressure. However, results from the non-smoker group, although containing only 4 subjects were surprisingly, opposite to those in the smoker group: significant increases in palm and finger temperatures along with decreases in heart rate and blood pressure triggered by cigarette smoking were measured, suggesting vasodilation of the skin's vascular bed. Further investigations into the underlying mechanisms and with a larger number of non-smokers, seems appropriate. In any case, the very strong and immediate impact of cigarette smoking on the human body can be clearly and impressively demonstrated, which might provide an additional form of motivation for smokers to give up smoking.

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