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Design and validation of an ambulatory system for the measurement of the microcirculation in the capillaries: μHematron device

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Abstract— **The non-invasive Hematron sensor is an active sensor used in studying skin blood flow (SBF) by measuring thermal conductivity of living tissues. Up to now, the Hematron device was composed of the Hematron probe and a heavy analog conditioning electronics. This paper presents the design, realization and validation of an ambulatory device (μHematron) associated with the original Hematron probe. The electronic architecture is based on a Programmable System on Chip (PSoC^{TM}), which contributes in reducing the number of discrete components, and consequently, the electronic conditioning circuit of Hematron. The μHematron device can be worn on the wrist of the patient thanks to its size ($4\times3\times1cm^3$) compared to the non-ambulatory conditioning electronics sized $20\times30\times20cm^3$. In addition, data can be stored in a μSD card or transmitted using a ZigBee module. The validation of the μHematron device was performed using the analog conditioning electronics as a reference. Experiments were performed first on a physical model reproducing microcirculation in order to characterize the linearity of the thermal conductivity as a function of water flow. Then, two experiments were hold in-vivo conditions highlighting the performances of this new device. In a first experiment, effects of mental calculation on effective tissue perfusion were measured and in a second one, effects of an anti-cellulite cream on micro-vascularisation and skin temperature were studied.**

I. INTRODUCTION

In health care technology, it is important to miniaturize the devices to make them convenient to carry or wear and thus suitable for ambulatory monitoring applications. Skin temperature and thermal conductivity are among important parameters in ambulatory monitoring and are used in the study of emotional reactivity and the general health status of the patients.

The thermal conductivity of a tissue is directly related to thermal exchanges. These exchanges depend on the effective blood perfusion of the tissue. Thermal conductivity measurement is indicative of skin blood flow and it is considered as an indication of such tissue perfusion [1]. We present in this paper, recent work carried out on the miniaturization of the electronics associated with the original Hematron probe [2] used for skin blood flow measurement (dimensions of the electronics of μHematron: 3x4x1cm^3). The new design of the associated electronics (μHematron) is based on a programmable component, PSoC^{TM}[3], which enabled us to reduce the number of external discrete components and thus minimize the hardware to facilitate ambulatory measurements by locating the total miniaturized system comfortably on the patient's wrist. Fig. 1A.

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II. BACKGROUND

Skin microcirculation is key parameters in many clinical applications and several methods have been developed are presented below with their relative advantages and disadvantages. Note, the isocaloric and isothermal methods are both based on the thermal clearance method, introduced by Gibbs in 1933 [4], [5].

A. Isocaloric method

Constant electric power is applied via a voltage source supplying a heating electrical resistance. In this method, blood flow is measured by the dissipation of temperature tissue underlying. Reading the difference of the temperature between the rings of thermocouples gives an image of the skin microcirculation.

Advantages: easy to use, cheap, the measurement signal is independent of the thermal properties of the probe.

Disadvantages:

1) The nonlinearity of the measurement: many authors using this method take the heat as an index of tissue blood flow. However, the heating is inversely proportional to the thermal conductivity of the tissue.
2) The response time of the probe is approximately several seconds.
3) Variable value of heating of the tissue: the lower the thermal conductivity; the more heating [5].

B. Isothermal method

The electronic parts associated with the sensor are much more sophisticated than in the isocaloric method [6]. The electrical current needed to heat and maintain the tissue temperature constant must be controlled. The measurement of the electrical heating power is requested and is achieved by an electric device calculating the power dissipation at any time [5].

Advantages:

1) Linearity of the measurement: the dissipated electrical power is proportional to tissue thermal conductivity.
2) Speed of response: the response time of the probe is very low ($\prec$ 0.1 s) as it includes a feedback control system.
3) Constant value of heating (2^{o}C): constant heating gives rise a constant thermal field around the probe and avoids excessive tissue heating. As a consequence of

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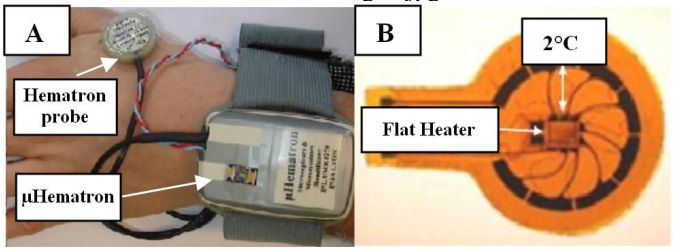

Fig. 1. A: The miniaturized Hematron system on a patients wrist. B: Hematron probe: the heating element is at the center of the disc, 8 thermocouple junctions are located at the periphery of the disc.

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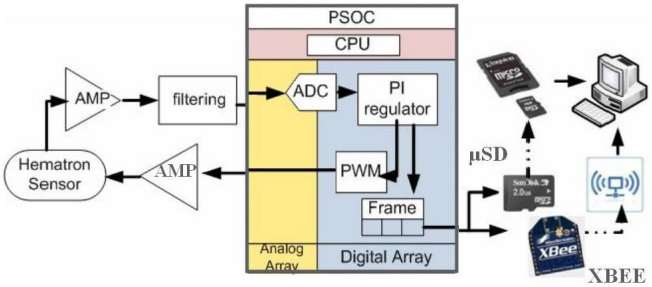

Fig. 2. The conditioning electronics of μHematron with PSoC.

the constant field, the volume explored by the probe depends directly on the thermal conductivity of tissue.

Disadvantages:

1) Complex electronics (a feedback control system is required).
2) It is sensitive to temporal variations in the tissue thermal gradient.

C. Laser Doppler flowmetry (LDF)

The surface of the skin is illuminated with low power laser light [7]. LDF is based on the Doppler shift of back-scattered laser light. It is a non-invasive technique capable of instantaneously and continuously assessing local blood flow in tissue. The light scattered back from the tissue is collected by one or more additional optical fibers and analyzed.

Advantages: LDF is cheap, easy to use, does not require specialist training, helps in diagnosing vascular disease, and can be used on any area of skin [8].

Disadvantages: the depth of application of laser Doppler is limited by its wavelength. Its use on other regions beyond the skin is therefore limited. Additionally, its spatial resolution is limited, measurements are extremely local and the units of measurement are arbitrary [9].

D. Thermal Conductivity

Thermal conductivity (k) is the heat quantity (Qh) per unit of time (dt) flowing from the hot side to the cold side of a volume for a fixed area (A), a fixed inter-surface distance (dX), and a fixed inter-surface temperature difference (dT).

$$k = \frac{Qh\ dX}{A\ dt\ dT}$$

Thermal conductivity has units of mW/cm.^{o}C and values range from 2 to 9 for biological tissues. The thermal conductivity of the skin has been observed to increase linearly with the skin blood flow [10].

III. PROBE AND INSTRUMENT SYSTEM

A. Hematron Probe

The Hematron probe consists of a disc 25 mm in diameter and 4 mm thick. The measuring surface, which is in contact with the skin, is composed of two parts: the reference part at the periphery of the disc and the measuring part at the centre of the disc. The difference in temperature between the measuring part and the periphery part is measured by means of 8 copper-constantan thermocouple junctions. A planar flat thermal heating element is located in the central part of the sensor; it consists of a 120Ω constantan resistor. A proportional integral PI regulator controls the heating power in the central heater so that a constant difference of 2^{o}C is maintained between the measuring and reference components. The thermal power required to maintain this difference in temperature is proportional to the thermal conductivity [10],[11]. Fig. 1B

B. Conditioning Electronics

The conditioning electronics of the Hematron probe, Fig. 2, is based on a Programmable System on Chip, PSoC. These mixed signal (analog/digital) circuits comprise a microcontroller as well as analog digital blocks. A PSoC can integrate up to 100 peripheral functions (analog filters, amplifiers, converters, PWM, UART, etc), thus reducing the time for the design, the power consumption and the cost of the system [3].

For the μHematron device, the majority of analog electronic components are located outside of the PSoC due to the differences in the operating values required and analog components inside the CY8C29466 PSoC (16 digital blocks and 12 analog blocks); however the number of the digital functions remained the same. An amplifier with gain of 2200 was used in the processing of an input voltage of 640 μV (T = 2^{o}C) at 1.4V. The amplified signal was filtered by an anti-aliasing filter with a cut-off frequency of 5 Hz for a sampling frequency of 10 Hz. The amplification and the filtering were not integrated into the PSoC as a result of their differing parameter settings (cut-off frequency, gain) which exceeded the limits for internal components. The PSoC includes a 12 bit analog/digital converter which digitalized the signal used by the PI regulator (resolution: 1/868^{o}C). The signal of the regulator controlled the heating element through Pulse Width Modulation (PWM) with a 16 bit resolution. The power supplied to the heating element is the direct image of skin thermal conductivity. The data was stored locally on a SD memory card and transmitted wirelessly ZigBee (MAXSTREAM-XB24-BCIT-004). The XBEE (ZigBee protocol) module was chosen for its low power consumption, small size and it facilitated

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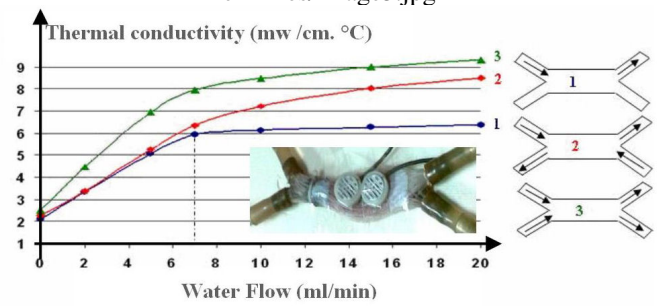

Fig. 3. Relationship between thermal conductivity of a perfused physical model and simulated skin blood flow for 3 cases: (1) only one bed of capillaries was perfused, (2): the two beds of capillaries were perfused in opposite directions, (3): the two beds of capillaries were perfused in the same direction.

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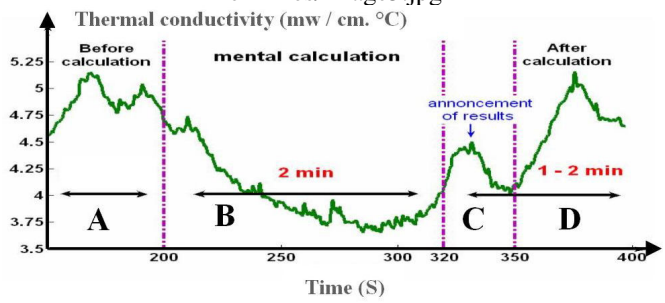

Fig. 4. Effect of mental calculation on skin blood flow: during the mental calculation (B), the microcirculation decreases. Announcement of the results (C). At the end of the experiment, the microcirculation increases (D) and the initial level (A) is reached after 2 minutes

communication (serial protocol UART).

IV. RESULTS

A. Thermal conductivity calibration

The calibration of the sensor was performed using physical models such as Vaseline and Polyacrylamide gel, whose thermal conductivities are known and stable (1.73 and 5.93 mW/cm.^{o}C, respectively). The parameters of the digital PI regulator (*Kp*: the proportional part, *Ti*: the integral part) were optimized to have the best speed-stability and the lowest measurement noise.

B. Experimentation on Physical Model

The following tests were performed on a physical model of microcirculation using water flow to characterize the linearity of the thermal conductivity as a function of the water flow. The physical model consists of 2 groups of 100 catheters (0.7 mm outer diameter, 0.3 mm inner diameter), each group perfused independently Fig. 3. The reference analog electronics and the new miniaturized electronics were used with two Hematron probes. The perfusion combinations used are indicated on Fig. 3 Results for both probes were very similar with regard to their relation between thermal conductivity and water flow. Only results obtained with the new instrumentation are therefore presented. The perfusion of a single group of catheters (case 1 - curve 1) led to linear increase in thermal conductivity (0-5 ml/min). Perfusion in the same direction for both groups (case 3 - curve 3) leads to an increase in thermal conductivity, i.e higher than for a single group. The most important result, however, is obtained when the two groups are perfused simultaneously and in opposite directions (case 2 - curve 2), the increase in thermal conductivity is lower than for case 3-graph 3, but with a larger linear section (up to 7 ml/min, as shown).

C. Experimentation in Vivo

1) Mental Calculation: We studied the effect of mental calculation on skin blood flow. The Hematron probe was attached on the left hand of 25 year old subject in a normal state of vigilance, while in a seated position and in thermal comfort. The subject placed his left hand on a table for 3 to 4 minutes (Fig. 4A), and then carried the mental calculation for 2 minutes (B). During the measurement and under steady state conditions, skin blood flow of the subject is not constant and fluctuates with time.

Skin blood flow can be considered as an activation index [12] and more generally as an index of the emotional reactivity. Therefore, at the beginning of the mental calculation, the skin blood flow decreases traducing a peripheral vasoconstriction. Oscillations observed on the skin blood flow are related to the heart rate (period of 1s), respiration rate (period of 4 to 5s) [13]. Two others kind of labile oscillations also exist with a period of 10s and 60s, the longer ones are observed for subjects in a sensorimotor rest, traducing their relaxation state.

It was reported that these oscillations disappear during mental calculation; this corresponds to the phase B on the Fig.4. Indeed, oscillations are stopped (after several minutes) by an external stimulus and start again at the end [14].

2) The Local Effects of Cosmetics: In cosmetology, the measurement of the skin blood flow is an essential tool to measure and assess the effect and/or the efficacy of a product on micro-vascularisation. The test was performed to highlight the effect of an anti-cellulite cream on microcirculation in the capillaries. The thermo-active effect of this cream accelerates the microcirculation for a prolonged period by a heating and

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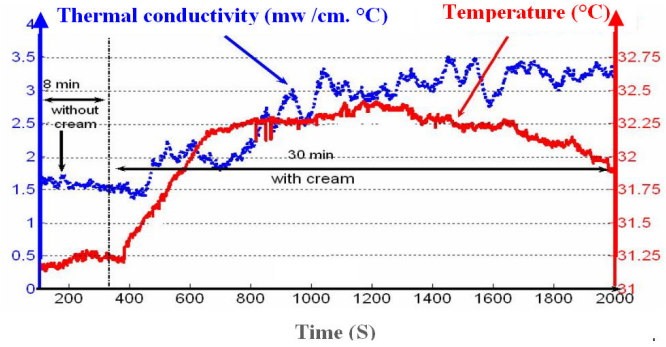

Fig. 5. Effect of a anti-cellulite cream on skin blood flow and on the skin temperature of the left forearm, A: microcirculation and the temperature before applying the cream were stables, B: both the microcirculation and the skin temperature increased following application of the cream

a reddening of the epidermis, its intensity and its duration have been reported to vary according to skin types. [15]
We spread a thin layer of this cream base caffeine on the skin of the left forearm of 20 year old subject in a room at 25^{o}C ambient temperature (stable during the experiment). The Hematron probe and a thermistor were placed on the forearm immediately following the application of the cream. The thermal conductivity of the arm and the skin temperature were recorded. The microcirculation and the skin temperature before applying the cream were stable. Few minutes following application of the cream, both the microcirculation and the temperature increased. Skin temperature varied significantly (0.24^{o}C/min) during 4 minutes, remained quite constant during 15 minutes and then started to decrease. Approximately fifteen minutes after the application of the cream, vasodilatation was at its maximum (about twice the initial value). Fig. 5

V. CONCLUSIONS

The miniaturization of the device and the reduction in power consumption has no adverse consequence on the system's performances. The experiments carried out with the new μHematron device show that characteristics are comparable with those of the (reference) analog electronics. The final size of the electronic layout is compatible with the development of wrist-worn device, suitable for ambulatory monitoring. Data are stored on a μSD card or transmitted using ZigBee module. The μHematron's electrical consumption was 130 mA at 3.7 V (5 W) which is well below the 10 W consumption of the analog conditioning electronics. The possible field of applications for the μHematron is wide: cosmetics (moisturizing creams, allergic reactions), pharmacology (vasodilators), functional studies (microcirculation), the prevention of pressure ulcers and combined studies involving the activity of the autonomous nervous system such as the study of car driver vigilance under real driving conditions.

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