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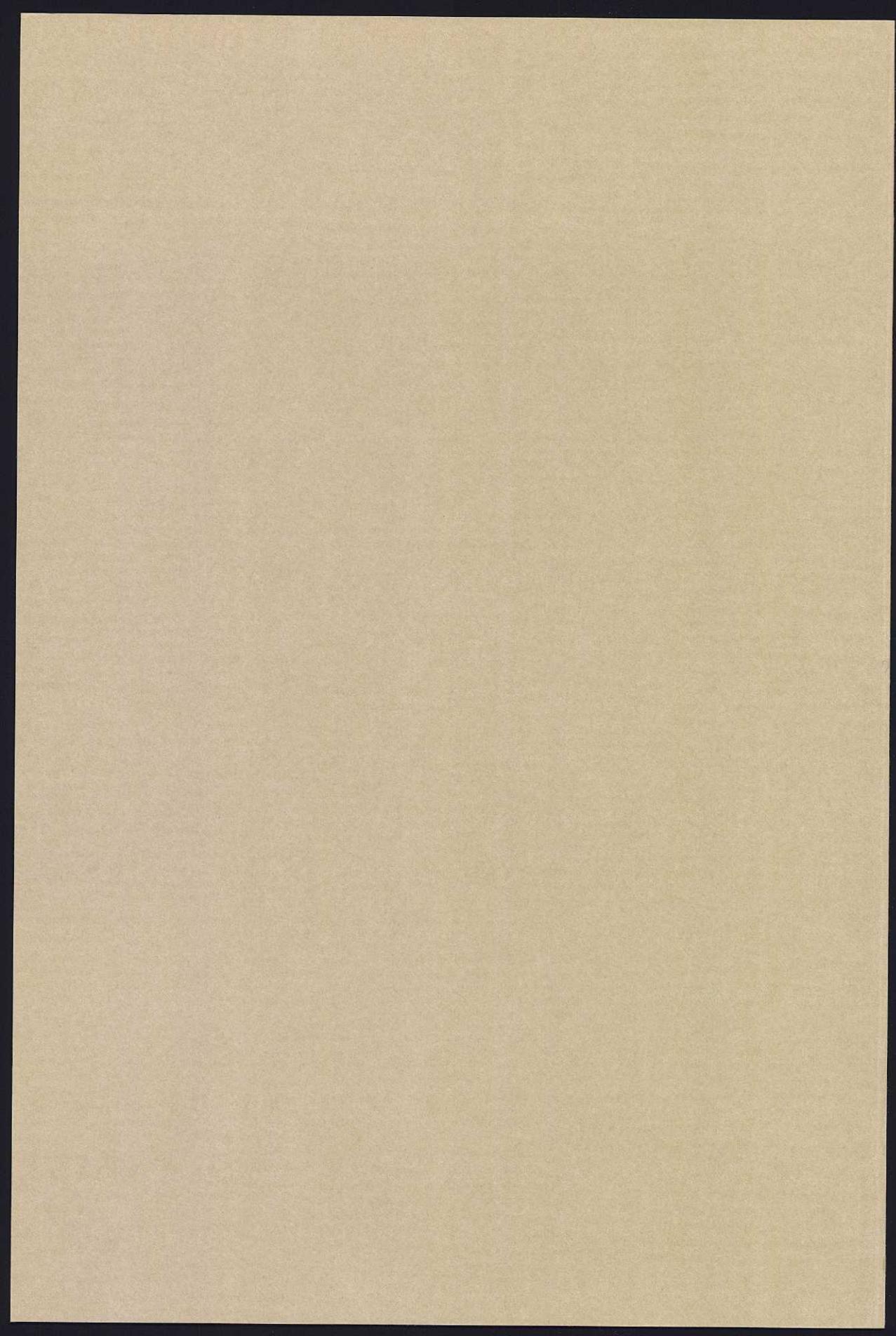
# Skin Temperature over a Localized Heat Source

An experimental study with reference to the clinical use of  
infrared thermography

By

KRISTER NILSSON

GÖTEBORG 1974



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av

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GÖTEBORG 1974



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The present thesis is based on the following publications:

1. Surface temperature over an implanted artificial heat source. In press, 1974, Phys. Med. Biol., 19, Nr. 5. (Together with S.E. Gustafsson).
2. Analytical calculation of the skin temperature distribution due to subcutaneous heat production in a spherical heat source. To be publ. in Phys. Med. Biol. (Together with S.E. Gustafsson and L.M. Torell).
3. Skin temperature over an artificial heat source implanted in man. To be published in Phys. Med. Biol.

## CONTENTS

1. Introduction	7
2. Aims of the present investigation	9
3. Skin temperature - a subtle balance of physiology and physics	10
3.1. $H_C$ Conductive heat flow	11
3.2. $H_B$ Convective heat flow	12
3.3. $H_R$ Radiative heat loss from the skin surface	14
3.4. $H_F$ Convective and conductive heat loss from the skin surface	14
3.5. $H_E$ Evaporative heat loss from the skin surface	15
4. Skin temperature measurements	16
4.1. Contact surface thermometry	16
4.2. Radiometric surface thermometry	17
5. Experimental methods and comments on methods	24
5.1. Quantitative surface temperature measurements with infrared thermography	24
5.2. An implantable artificial heat source	28
5.3. Properties of the artificial heat source tested in vitro	29
5.4. Experimental procedure with implanted heat sources	30
5.5. Methods for measurement of the distance between the heat source and the skin surface	32
5.6. Methods for definition of the tissue surrounding the heat sources	32
6. Theoretical analysis of the temperature distribution on the surface over a heat source	33

7.	Results and comments	35
7.1.	A theoretical description of the surface temperature distribution over a heat source in living tissue	35
7.2.	An experimental model for quantitative studies of the surface temperature distribution over a heat source in living tissue	35
7.3.	The skin temperature over the artificial heat source as a function of the heat source power and position	39
7.4.	The influence of varying environmental conditions on the skin temperature distribution over the heat source	42
8.	Heat production and heat distribution in living tissues and in the experimental model	44
8.1.	Heat production	44
8.2.	Heat distribution	47
9.	Summary and conclusions	50
	References	52
	Original publications:	
	Surface temperature over an implanted artificial heat source	55
	Analytical calculation of the skin temperature distribution due to subcutaneous heat production in a spherical heat source	73
	Skin temperature over an artificial heat source implanted in man	85

## 1. Introduction

Every process of life results in energy production. Energy production is intimately connected with the concept of temperature.

Estimation of the temperature of different surface areas of the body - in practice, the skin temperature - is a very much older diagnostic aid than measurement of the so-called body temperature. Thus, Hippocrates taught his pupils that "cold head, hands and feet, warm breast and abdomen constitute an omen malum for the patient" and also recommended the physician to "examine to see whether one side is hotter than the other" (quotations from, among others, Foged 1932 and Bowling Barnes 1968). The five Celcussian cardinal symptoms of an inflammatory reaction are even better known - "Calor, rubor, tumor, dolor et functio laesa".

Ever since the invention of the gas thermometer by Galileo Galilei in the late sixteenth century, a quantitative measurement of temperature has been possible. The introduction of thermometry as a routine procedure in clinical medicine has been attributed to Carl Wunderlich about 1870.

For a century body temperature has been used as an extremely valuable diagnostic, prognostic and even therapeutic aid in clinical medicine.

No corresponding method for the quantitative measurement and use of local surface temperature changes has been available. The development of electronic contact thermometric and point radiometric surface temperature measurement instruments has mainly been applied to physiologic and bioclimatological research. Routine clinical use of skin temperature measurements concerns clinical physiology and peripheral circulatory disturbances. However, various techniques of skin temperature measurements have been employed for clinical judgement of shock, rheumatoid arthritis, skin diseases etc.

The introduction of scanning radiometers, so-called infrared thermographic (IRT) instruments, presenting a pictorial illustration of the temperature over a surface, has resulted in increased interest in local temperature changes of the skin overlying different pathological conditions.

The pioneering work by Lawson (1956) presented an entirely new possibility of detecting breast tumours, by means of skin temperature measurements. This was a very attractive field, which might explain the enthusiasm with which this new method was welcomed. This medical use is probably still the predominant one, but IRT has been tried in almost every clinical discipline.

Surveys of the medical use of IRT have been published by, among others, Gershon-Cohen, Haberman and Brueschke (1965), Bowling Barnes (1968), Maxwell-Cade (1968), and Young (1970). Symposia on IRT have been held in New York (1964), Strassbourg (1967) and Leiden (1969).

IRT has been applied to breast cancer diagnosis, peripheral circulatory disturbances, cerebral circulation, superficial tumours, cutaneous diseases, rheumatoid arthritis, burns, placental localization, ophtalmic diseases, and thyroid diseases.

Most of the clinical reports have been correlative. Thermography has been compared to other well-documented diagnostic methods. Studies of the mechanisms underlying the registered surface temperature changes are however comparatively sparse.

The growing interest for clinical use of IRT in breast disease diagnosis but also for other clinical applications is partly based on the original idea by Lawson and Chughtai (1963) postulating an increased metabolism in malignant and inflammatory tissue transferred to the overlying skin by conduction in the tissue and convection in the vessels draining the tumour. The present work is a theoretical and experimental study of the physical and geometrical parameters influencing the skin temperature over a localized heat source.

This work is the result of an interdisciplinay co-operation between the Department of Anatomy, University of Gothenburg and the Department of Physics, Chalmers University of Technology.

## 2. Aims of the present investigation

This work presents an experimental and theoretical analysis of the skin temperature distribution over a heat source in living tissue.

The aims of the work are

1. to give a theoretical description of the surface temperature distribution over a heat source in living tissue;
2. to develop an experimental model for quantitative studies of the skin temperature distribution over a heat source in living tissue;
3. to study the skin temperature as a function of the power and the position of the heat source;
4. to study the influence of varying environmental conditions on the relation between the skin temperature and the heat source power and position;
5. to compare the experimental and theoretical results with available data on heat production and distribution in living tissue in order to evaluate the possibility to use skin temperature measurements as an indication of an underlying pathological process.

The study is directly pertinent to the clinical use of IRT for breast cancer diagnosis but also deals with the general relation between skin temperature and the condition of the underlying tissue.

The aim of the work is to offer experimental and theoretical information on heat distribution in living tissue, supplementing the growing clinical experience of IRT.

### 3. Skin temperature — a subtle balance of physiology and physics

The body temperature as measured at the receptor site, i.e. in the hypothalamus, is one of the well-controlled homeostatic parameters. In contrast to this, the skin temperature reveals considerable variations, both when different parts of the body are compared, and when the same area is studied during a certain period of time. Variations in local skin temperature are registered even at a constant ambient temperature (Honma, Kimura, Harada and Sekine 1966). This is a consequence of one of the main functions of the skin, namely to act as an effector organ in the body temperature regulation.

It is not within the scope of this presentation to discuss the complex mechanisms involved in body temperature regulation as a physiologic and bioclimatologic problem. An extensive survey of this problem has been presented by Hammel (1968) among others.

The skin temperature as a result of physiological and physical influences is diagrammatically summarized in Fig. 1 (Brånemark and Nilsson 1969, after a suggestion by Prof. R. Skalak, New York). The figure illustrates the multiplicity of factors influencing the skin temperature ( $T_S$ ). Metabolic heat production ( $Q_M$ ) and heat conveyed to the area by blood vessels ( $Q_B$ ) are conducted ( $H_C$ ) and convected ( $H_B$ ) to the skin. Normally heat is lost from the skin by radiation ( $H_R$ ), by conductive and convective heat flux to the surrounding air ( $H_F$ ) and by evaporative heat loss ( $H_E$ ).

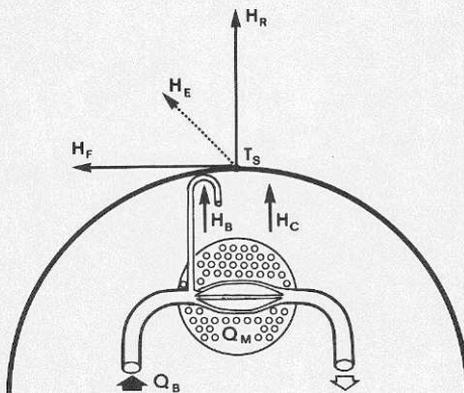


Fig. 1. Diagrammatic summary of factors involved in the heat flux at the skin surface. The homeostatic situation at the point  $T_S$  can be expressed:  $H_B + H_C = H_R + H_F + H_E$ .

An extensive presentation of these different parameters from physiologic and bioclimatologic aspects is given by Tregear (1966). Hensel (1952) summarizes the heat transport in superficial tissues, providing a background for the science of thermoreceptor physiology. Data on the thermal "constants" for superficial tissues have also been reviewed by Henriques and Moritz (1947), Lipkin and Hardy (1954), Stoll (1960), and Haberman, Francis and Love (1972). Draper and Boag (1971a,b) have also presented a review of these "constants" as a basis for a theoretical calculation of the surface temperature distribution over point and line heat sources.

The following discussion is mainly based on these references, additional ones being cited in the text.

### 3.1. *HC Conductive heat flow*

The skin temperature is dependent on heat distribution in the skin itself, in the subcutaneous fat and in the underlying muscular tissue.

For the steady state situation, thermal conductivity is the only physical parameter affecting the heat distribution, in contrast to non-steady states, where the heat capacity and density of the material must be taken into account.

Measurements of the thermal conductivity of the three tissue components reveal considerable variation. This is to be expected, since, ideal physical measurements can only be performed on excised specimens, which may introduce artifacts. The conductivity of the tissues in situ can be calculated with indirect methods analysing heating or cooling events.

The range of the thermal conductivity of the respective tissues as reported in the literature are

Subcutaneous fat	0.2 - 0.3	W/m <sup>0</sup> C
Skin	0.4 - 0.7	W/m <sup>0</sup> C
Muscle	0.4 - 0.8	W/m <sup>0</sup> C

It must be emphasized, however, that the heat distribution in living tissue with intact circulation is always a result of the specific thermal conductivity of the tissue and the convective heat distribution with the circulation. This combined heat distribution parameter is usually referred to as the effective thermal conductivity.

### 3.2. $H_B$ Convective heat flow

The convective heat transport can be described as a function of the blood flow, the specific heat of the blood, the temperature fall of the blood when passing the tissue, and an exchange factor. The last parameter is difficult to estimate and, consequently, the magnitude of the convective heat distribution difficult to quantify.

In discussing convective heat flow, a division into non-directional and directional flow is useful. This is an arbitrary division, where a non-directional heat flow is said to take place in a vascular network, such as the subpapillary vessels in skin, and a directional heat flow can be illustrated with the heat distributed along macroscopically visible vascular pathways, such as a subcutaneous vein. By definition heat convection without direction cannot exist. The term "non-directional" is only intended to describe a convective heat transport taking place over a tissue via numerous vascular channels that cannot be macroscopically defined. The net effect of this convection, however, generally has a certain direction, e.g. the transport of heat from the body core to the skin surface expressed as a "thermal circulation index" (Burton 1948).

#### Non-directional heat convection

The blood flow of skin is controlled by both central and local factors.

Blood flow variations serving the body temperature regulation are mainly effected by the hypothalamic centre. The constricted skin circulation at hypovolemia and alarm reaction is also an expression of a central control mechanism. Pale and cold skin illustrates the close relation between skin circulation and skin temperature.

It is also obvious that local mechanisms influence the skin circulation - e.g. the triple response or the hyperemia at sunburn. Local heat and skin circulation are closely connected (Hertzman 1961). A local skin temperature increase from

30°C to 40°C will result in increased skin circulation. This will, in turn, give rise to a threefold to fourfold increase of the effective thermal conductivity of the skin (Hensel 1952, Lipkin and Hardy 1954).

Values of the effective thermal conductivity of skin must be estimated with this interrelation of heat and thermal properties being taken into consideration.

#### Directional heat convection

Heat transport in large vessels plays an important role for the dissipation of heat from a circumscribed tissue volume, e.g. from active muscles to the overlying skin surface (Cooper, Randall and Hertzman 1959). The same mechanism has been postulated for breast tumours (Lawson 1956, Lawson and Chughtai 1963, Freundlich, Wallace and Dodd 1968, Draper and Jones 1969, Dodd, Zermeno, Marsch, Boyd and Wallace 1969, Draper and Boag 1971b, Feasey, Davison and James 1971, Haberman, Francis and Love 1972, Barash, Pasternack, Venet and Wolf 1973).

The channels available for directional heat flow from, e.g., a mammary tumour consist mainly of the draining veins. The vascular topography of this venous system is highly variable (Massopust 1948, Massopust and Gardner 1950, Feldman 1969). Furthermore, the blood flow is affected not only by general physiological mechanisms but also by specific hormonal changes. The direction and magnitude of the heat distribution in this vascular system are obviously very difficult to register or calculate.

From a theoretical point of view very steep temperature gradients should be registered over superficial veins (Draper and Boag 1971a,b). This has been confirmed in experimental measurements of the temperature distribution over the superficial vessels of, e.g., the rabbit's ear, which reveal a gradient of about 0.5°C/mm perpendicularly to the vessel (Brånemark and Nilsson 1969). A very distinct influence of superficial vessels on the thermal pattern over implanted artificial heat sources has also been experimentally demonstrated (Nilsson and Gustafsson 1974)

### 3.3. *H<sub>R</sub> Radiative heat loss from the skin surface*

The net radiative heat loss from a surface can be calculated according to the Stefan - Boltzman formula (see Chapter 4:2).

The radiative heat loss is related to the surface temperature, the ambient temperature and the emission characteristics of the surface.

At a room temperature of about 20°C and a surface temperature of about 35°C the net radiative heat loss is about 6 W/m<sup>2</sup> °C for an ideal black body. The influence of the surface emissivity is of fundamental importance for IRT registrations and is discussed in Chapter 4.2.

### 3.4. *H<sub>F</sub> Convective and conductive heat loss from the skin surface*

The combined convective and conductive heat loss from the skin surface is considerably more difficult to measure or calculate than the radiative heat loss.

When the air over naked skin is forced to move, convective heat loss dominates. The increase in convective heat loss at forced convection is approximately proportional to the square root of the wind speed.

The convective and conductive heat loss from a surface can be estimated from registrations of the temperature gradient in the air perpendicularly to the surface. From a series of temperature measurements the gradient can be extrapolated to an "effective still air layer" representing the thickness of a layer of still air that should offer the same insulation as the actual moving air. The "effective still air layer" multiplied by the known thermal conductivity of air (0.023 W/m°C) will then give the actual heat flux from the surface.

The approximate values for the conductive and convective heat flux from a vertical skin surface at increasing wind speeds have been given by, among others, Draper and Boag (1971a):

wind still	4 W/m <sup>2</sup> °C
0.2 m/sec	5 W/m <sup>2</sup> °C
2 m/sec	17 W/m <sup>2</sup> °C

### 3.5. $H_E$ *Evaporative heat loss from the skin surface*

At a normal ambient temperature and at rest this heat loss is considerably smaller than the approximately equal radiative and conductive - convective heat losses. Less than  $1 \text{ W/m}^2 \text{ }^\circ\text{C}$  is lost by evaporation in connection with perspiratio insensibilis.

During intense perspiration or at artificial cooling with volatile agents, the evaporative heat loss may reach values around  $60 \text{ W/m}^2 \text{ }^\circ\text{C}$ . This heat loss parallels the heat transport capacity of skin, making possible heat loss corresponding to 15 times the basal metabolism from the total body area. This reserve capacity makes body temperature regulation possible in extreme environments, but it also makes it difficult to estimate the effect of artificial cooling.

#### 4. Skin temperature measurements

Although the skin is so easily accessible an exact measurement of its surface temperature is difficult.

An extensive discussion of various techniques has been presented in a series of papers by Hardy (1934), by Stoll and Hardy (1949, 1950) and by Stoll (1964).

In principle, skin temperature measurements can be performed with contact thermometers or with radiometers.

##### 4.1. *Contact surface thermometry*

Numerous designs and function principles for contact thermometry probes have been presented. The handling and registration technique is simple, bringing a sensor element - usually a thermocouple or a thermistor - into contact with the surface.

There are, however, certain obvious sources of error affecting the accuracy.

From a purely physical point of view the heat sensitive body, e.g. the thermistor, is influenced by the surface temperature but also by the temperature of the sensor support and by the surrounding air. The sensitive body can be shielded from these influences. It must be emphasized, however, that such a shielding disturbs the heat balance of the surface and that the results are not representative of the naked skin surface.

A second source of error is the heat loss from the surface along the leads and the support of the sensor. This heat loss does not only influence the mean temperature of the sensor, but may also lower the surface temperature. Very thin leads and isolating support reduce this artifact. The leads and support can also be placed parallel to the surface in order to reduce the heat flux, which is dependent on a temperature gradient. Advanced feed-back systems, with electronic compensation for the initial temperature difference between the probe and the measured surface, can also prevent heat transport in the probe (Kalliomäki and Wallin 1971, Stekete 1973).

A high and constant contact pressure between the sensor and the surface is required for stable measurements. The necessary contact pressure will give rise to physiological

changes in the local skin circulation. As the necessary contact pressure for a stable thermocouple reading has been shown to exceed the systolic blood pressure (Stoll and Hardy 1950), a local ischemia under the sensor will result. According to these authors, however, the net effect of the contact pressure will be a successively increasing temperature. This increase can be attributed to the fact that the compression brings the heat source "into contact" with deeper tissues, but also to a local tissue injury that provokes an inflammatory reaction with hyperemia in the surrounding tissues. A temperature increase of  $2^{\circ}\text{C}$  has been measured for thermocouples at the contact pressure necessary for stable registrations.

The spatial resolution achievable with contact thermometry is dependent on the dimensions of the probe and the possible number of registrations per unit area. It is obvious that contact thermometric mapping of the temperature of a skin surface necessitates numerous measurements with a careful technique concerning probe design and contact pressure.

## 4.2. *Radiometric surface thermometry*

### Fundamental radiation physics

Radiative surface temperature measurement makes use of the infrared spectral band.

The definitions of various parts of the electromagnetic spectrum are more or less arbitrary. The IR spectrum is thus defined with an upper limit of  $1000\ \mu$  (extreme IR) and a shortest wavelength of  $0.75\ \mu$ , which is just above visible light.

For the IR spectrum as well as other parts of the electromagnetic spectrum the radiation can be characterized in terms of mathematical formulas.

The fundamental description of the radiation character is valid for a "black body", defined as an object absorbing all radiation that falls upon it at any wavelength.

On the basis of such an ideal black body radiator, the spectral energy distribution can be described by the Planck equation

$$Q_{\lambda b} = \frac{2 \pi h c^2}{\lambda^5 (e^{hc/\lambda kT} - 1)} \quad (\text{W/cm}^2)$$

where  $Q_{\lambda b}$  is the spectral radiant emittance within a spectral interval of  $1\mu$  at a specified wavelength for a black body and  $c$  is the light velocity,  $h$  is Planck's constant,  $k$  is Boltzman's constant and  $T$  the surface temperature in K.

The wavelength at which maximum emittance takes place, depending on the object temperature, can be calculated according to Wien's Displacement law

$$\lambda_{\max} = \frac{2898}{T}$$

The common observation that glowing objects change their colour from long wavelength red to shorter wavelength yellow at increasing temperature is thus mathematically expressed by this formula. The wavelength corresponding to maximum emittance for a perfect black body at 300 K (27°C), i.e. skin, is thus about 10  $\mu$ .

By integrating Planck's equation from  $\lambda = 0$  to  $\lambda = \infty$  the total radiant emittance is obtained. The result of the integration can be described by the Stefan - Boltzman formula

$$Q_b = \sigma T^4 \quad (\text{W/cm}^2)$$

where  $Q_b$  is the total emittance of a black body and  $\sigma$  is Stefan-Boltzman's constant.

This heat loss is compensated for by absorption of incoming radiation from the surrounding surfaces and the net radiative heat loss is described by

$$Q_b = \sigma (T^4 - T_A^4) \quad (\text{W/cm}^2)$$

where  $T_A$  is the ambient temperature.

For a non-ideal black body the emissivity of the surface ( $\epsilon$ ) influences for radiation exchange, modifying the equation into

$$Q = \epsilon \sigma (T^4 - T_A^4) \quad (\text{W/cm}^2)$$

Most detectors used in IR scanners are "photon" sensitive. The Planck equation can be transformed so as to give an expression of the number of photons /sec. area by means of the well-known relation of the energy of one photon =  $\frac{h \cdot c}{\lambda}$ , where  $h$  = Planck's constant and  $c$  = the speed of the light.

A derivation will give a peak photon emission at about 25% greater wavelength, for human skin at 27°C approx.  $12\mu$ .

In the discussion of various methods for recording IR radiation it should also be noticed that the "photon" detectors used in IR scanners are selective, i.e. they have a specified sensitivity range. Thus, the Indium Antimonide detector most commonly used has a sharp cut off at about  $5\mu$ . This sharp limit is explained by the fact that at greater wavelengths photons do not carry enough energy to excite electrons in the detector material.

A comparison between the sensitivity range of this detector and the wavelength spectrum in which human skin radiates ( $2-20\mu$ ) shows that the detector is capable of using only a few (2.4) percent of the radiation from the human skin at 30°C.

The very high sensitivity and short response time, however, compensate for this limitation.

The "short wavelength" detectors may be replaced by highly sensitive, fast detectors, with a wavelength sensitivity in the range up to  $10\mu$ , which are now available.

#### Radiometric skin temperature measurements

The use of radiation measurements of the skin temperature was initiated by Cobet and Bramigk (1924). The basis for its use in the biological and medical sciences was presented in a series of works by Hardy (Hardy 1934a,b,c, Hardy and Muschenheim 1934, 1936, Hardy, Hammel and Murgatroyd 1956).

The Stephan-Boltzman law applies to skin radiation. This means that the temperature of the surface can be calculated if the energy radiated from the surface is measured and the ambient temperature and emissivity of the surface are known.

For practical purposes the radiometric surface temperature measurement is usually performed as a comparative measurement, i.e. the instrument is calibrated against a radiation reference.

### Emissivity of human skin

In the original work by Hardy (1934c) the emissivity of human skin was estimated to be almost unity in the wavelength range relevant for the natural radiation from skin.

Further studies by Hardy (1939) confirmed an emissivity for skin of 0.98-0.99.

As a result of the growing interest in bioclimatology and especially with the development of infrared thermography for use in experimental and clinical medicine, the emissivity of skin has attained increasing importance.

Several authors have discussed the emissivity of skin on theoretical and experimental bases. Mitchell, Whyndham, Hodgson and Nabarro (1967) reviewed the problem and presented an emissivity measuring technique not necessitating a parallel skin temperature measurement. Special interest has been devoted to the emissivity of skin in the wavelength range of the Indium Antimonide detector ( $2-6 \mu$ ) used in most IR-scanners (Watmough and Oliver 1968a,b, 1969). These results as well as later results presented by Stekete (1973) indicate an emissivity of  $0.99 \pm 0.01$  for human skin, which is entirely consistent with the early works by Hardy et al. Inconsistent results, indicating a wavelength dependency for the emission factor of human skin between 1 and  $6 \mu$ , have been reported by Elam, Goodwin and Lloyd-Williams (1963).

A radiative surface temperature measurement of an imperfect black body, i.e. a surface with an emission factor less than unity, will give a temperature error. The magnitude of this error is dependent on the emission factor of the surface, the surface temperature and the ambient temperature. Theoretical calculations of the emissivity dependence of radiative surface temperature measurements have been presented by, among others, Wolfe (1964) and Watmough and Oliver (1968a). The temperature error in relation to an ideal black body of the same surface temperature can be calculated to be between 0.15 and  $0.7^{\circ}\text{C}$  per 1% emissivity variation, implying a surface temperature of about  $35^{\circ}\text{C}$  and an ambient temperature of  $20^{\circ}\text{C}$ .

An arithmetic calculation according to the following equation will give a reasonably accurate estimate of the relation between the emissivity variation and the temperature error.

$$\text{Temp.error} = \frac{\text{emissivity variation}}{\text{emissivity of reference surf.}} (\text{surf.temp.} - \text{amb.temp.})$$

Under the given conditions a temperature error of 0.15°C per 1% emissivity variation can be calculated.

Many biological objects display curved surfaces to the thermal scanning system. The variation in emissivity with the angle at which the surface is viewed has been theoretically calculated by Watmough, Fowler and Oliver (1970). If human skin is regarded as a dielectric surface, a temperature error of 0.5°C at an angle of 50 degrees and 4°C at an angle of 70 degrees to the normal could be calculated. An experimental test presented by Lewis, Goller and Teates (1973) indicates a less pronounced dependence of the viewing angle. A temperature error of less than 1.5°C was measured for viewing angles up to 75 degrees. The authors ascribe the divergence between the theoretical and the experimental results to the non-dielectric character of the human body and the fact that neither the human skin nor the test object used for the experimental measurements has an optically smooth surface.

#### Skin temperature measurements with scanning radiometers

Most commercially available IR scanners are built up around a high-sensitive IR detector. In principle, the surface temperature measurement is performed with an optical system searching the field of view, thereby successively focusing different parts of the object surface on to a detector or a set of detectors. The construction of the scanning system varies between different manufacturers, using mirrors and/or IR transparent lenses or prisms. A theoretical discussion of the factors determining the thermal and spatial resolution properties of IRT equipments has been given by Wolfe (1964).

A discussion of the compromise between the practical and theoretical requirements for the design of IR scanners has also been presented by Maxwell-Cade (1968). The incompatibility between these requirements can be summarized as follows.

From a theoretical point of view a maximum thermal resolution is, of course, obtained with a small total field of view, a large instantaneous field of view (resolution element) and a long scanning time.

From a clinical point of view the appropriate total field of view depends on the object to be examined. The instantaneous field of view should be small to give a good spatial resolution and the scanning time short to render scanning of moving objects possible.

Desirable design characteristics of a medical thermographic equipment have been given by Dodd, Zermeno, Marsh, Boyd and Wallace (1969) as a thermal resolution of  $0.1^{\circ}\text{C}$ , a scanning time less than a second and a variable focal distance with a dependent spatial resolution which, for a field of view of about 30 cm, should be about 2 mm. The importance of an adequate depth of field as well as of a real time recording system and a temperature reference is also emphasized.

The commercially available thermographic equipments are presented with approximately the characteristics given above. It is beyond the scope of the present work to discuss the properties of the various "thermographs" available. It should be observed, however, that the specifications of different thermographic units are not entirely consistent and that a standardized testing model for spatial and thermal resolution capacity is in general not used. Dodd, Zermeno, Marsh, Boyd and Wallace (1969) and Macey and Oliver (1972) have proposed various designs of slit plates for standardized testing of IRT equipments concerning thermal and spatial resolution. A similar model has been used by the author for such tests and also for registering the focal depth of the equipment used (Chapter 5.1).

To judge from theoretical considerations and experimental tests, a temperature accuracy better than  $\pm 0.2^{\circ}\text{C}$  appears difficult to obtain for skin temperature measurements. The spatial resolution capacity is entirely dependent on scanning speed, detector characteristics and field of view/focal distance and can thus only be specified in absolute terms for a defined measuring situation.

A high scanning rate will result in a registered temperature defect for small objects with steep temperature gradients. The critical dimensions can be theoretically and experimentally described (Macey and Oliver 1972). Data on the instrument used for the present study are reported in Chapter 5.1.

## 5. Experimental methods and comments on methods

### 5.1. *Quantitative surface temperature measurements with infrared thermography*

The outstanding capacity of radiometers for skin temperature measurements is well documented (Stoll and Hardy 1949). This capacity cannot, however, be transferred to scanning radiometers. In all quantitative IRT studies "machinery artifacts" must be considered (Nilsson 1970, Macey and Oliver 1972). Our experimental work is based on the following technique.

#### Radiation reference

In clinical or experimental work where the temperature reference has to be located in the field of view, an ideal black body radiator is usually difficult to handle. Specially designed references have been described by many authors, and the continuous temperature "fin" devised by Charles and Francis (1973) deserves special notice.

It may be required of a temperature reference for clinical or experimental use that it should have a temperature accuracy of  $\pm 0.1^{\circ}\text{C}$  for a reference temperature range of 25 to  $40^{\circ}\text{C}$ . Also, the temperature of the reference must be adjustable within this range in a few minutes.

In this study a reference consisting of a copper block surrounded by a heat coil has been used. A thermistor in the copper block and an electronic servo system automatically adjust the temperature of the reference. A platinum resistor is cemented on to one surface of the copper block and coated with "Nextel" 101-C10, 3M Comp. (Fig. 2). The normal emittance of the paint over the wavelength 6 -  $14\mu$  is 0.93 (Hall 1973). The platinum resistor permits continuous checking of the reference function and the temperature stability. The resistance, and thus the temperature of the surface, is registered with a precision multimeter (Schlumberger-Weston 1242), and continuously checked against a standard resistance. The electronic servo system with a proportional power output is capable of keeping the platinum resistance at a constant temperature within the accuracy of the measuring equipment ( $0.1\text{ Ohm}$  corresponding to  $\pm 0.1^{\circ}\text{C}$ ).

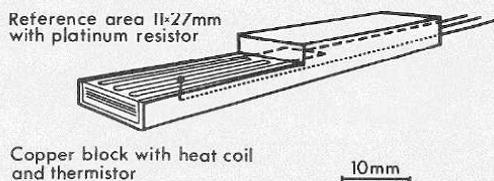


Fig. 2. Schematic drawing of the temperature reference, consisting of a copper block in a plexiglass support, a thermistor drilled into the copper block, a heat coil around the copper block, and a platinum resistor cemented on to one surface of the copper block. The reference area with the resistor is painted with Nextel<sup>(R)</sup> (3 M Comp.).

The reference is calibrated against an ideal black body radiator, the thermographic equipment being used as a zero temperature difference indicator in order to register the platinum resistor values for a few appropriate temperatures, e.g., 25, 30 and 35°C.

#### Calibration of the IRT instrument

An AGA Thermovision<sup>(R)</sup> mod. 669 is used for the surface temperature measurements. In our set-up the reference and a black body radiator are employed for calibrating the isotherm function of the IRT equipment. The reference is used as a temperature standard and set in an appropriate position on the isotherm scale by adjusting the picture black level (e.g., a reference temperature of 30°C covered by the isotherm set at 0.5). The isotherm scale is then calibrated for various temperatures of the black body radiator in relation to the reference at isotherm 0.5. The result of a calibration according to this method, with the temperatures and isotherm settings exemplified, is shown in Fig. 3. A temperature range of about 8°C is covered at sensitivity 10. The calibration technique presented gives a temperature accuracy of  $\pm 0.2^\circ\text{C}$  for objects in the focus plane and at the centre of the field of view.

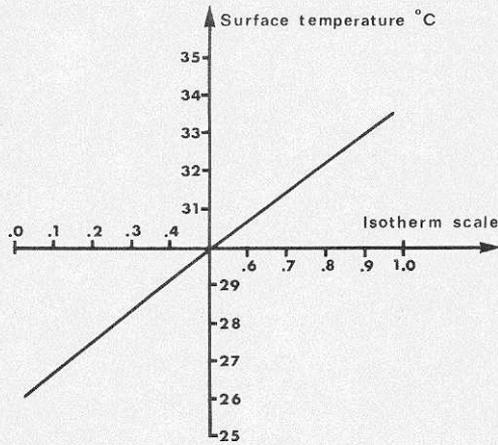


Fig. 3. Example of calibration of the isotherm scale (abscissa) against a temperature standard ( $30^{\circ}\text{C}$  black body temperature) at isotherm 0.5, sensitivity setting 10.

#### Influence of object size and defocusing on the thermal resolution capacity of the IRT instrument

The thermal and spatial resolution capacities of IRT instruments are of importance for their clinical and experimental use. Surprisingly steep temperature gradients are found over superficial vessels (Brånemark and Nilsson 1969). This finding is confirmed by theoretical calculations of the temperature gradient over a superficial line heat source, indicating a temperature fall of about  $0.5^{\circ}\text{C}/\text{mm}$  perpendicularly to the source (Draper and Boag 1971b). The experimental model introduced for studies of the temperature distribution over implanted heat sources may also result in steep temperature gradients. Macey and Oliver (1972) have presented an extensive theoretical and experimental account of the thermal and spatial resolution capacities of fast-scanning IRT instruments. A considerable loss of thermal resolution capacity was found for small objects.

An artificial test model, similar to the one proposed by these authors, was constructed in order to find the critical object size for the close-up version IRT used for the experimental studies. A slit plate, with slit widths of 5, 3, 2, 1,

and 0.5 mm, was placed over a constant-temperature surface. The temperature of these slits was registered by means of the isotherm function, with the slit plate in the focal plane and at successive defocusing. Full thermal resolution was found for all slit widths down to 2 mm in the focal plane. The true temperature representation was, however, lost for all slits at successive defocusing. A simple modification of the slit plate, with a plate having holes of 8, 5, 3, 2, and 1 mm in diameter, was used for studying the combined horizontal and vertical resolution. As regards the slit plate, the effect of successive defocusing was studied. Full thermal resolution was found for holes down to 3 mm in diameter in the focal plane. The temperature defects registered for holes of various diameters in the focal plane and at defocusing are shown in Fig. 4. A focal depth of about  $\pm 5$  mm could be estimated both for the slit and hole plate.

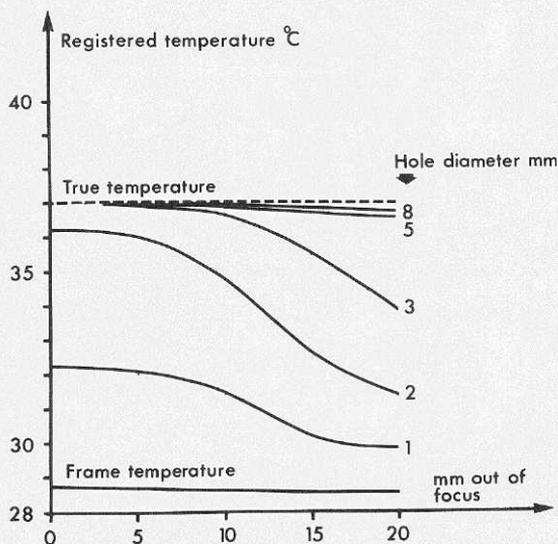


Fig. 4. Diagram showing the thermal resolution for circular objects of various diameters in the focal plane and at successive defocusing.

The picture element size for the close-up version of the Thermovision<sup>(R)</sup>, with a focal distance of 900 mm and a field of view of 65 x 55 mm, is about 0.6 mm. According to Macey and Oliver (1972), a theoretical calculation of the thermal resolution indicates a critical slit size of two to three

picture elements for a  $5^{\circ}\text{C}$  temperature increase, corresponding to a slit size of 1.2 to 1.8 mm in good agreement with the experimentally found 2 mm slit.

## 5.2. *An implantable artificial heat source*

If heat sources with variable and registrable heat output and temperature could be placed within the body at varying distances from the skin surface without causing adverse tissue reaction, such a model could be used for studying the relation between heat source power, position and the overlying skin temperature.

Tabern, Kearney and Dolbow (1966) presented a heat coil wound clinical thermometer introduced into the subcutaneous tissues or abdominal cavity of lightly anesthetized animals. This rather primitive heat source scarcely meets the above requirements.

Our experimental model is a development of a heat source, which could be implanted in a passive state and allowed to heal in the desired location. Interference with a tissue area at a distance from the implantation site for activation and registration should constitute an acceptable compromise between a difficult technical and biological problem.

In a preliminary experimental study button-like 11 x 4 mm heat sources were made of titanium and implanted in rabbits (Paper I).

In order to make a comparison between experimental and theoretical results more valid, a spherical titanium heat source with symmetrical heat output was designed and used for implantations in animals and man. The modified heat source is described in paper III. In principle it consists of a heat coil and a thermistor mounted in a titanium sphere with an outer diameter of 4.5 mm. The electrical leads to the sphere are encapsulated in an 80 x 2 mm silicone tube. The construction materials were chosen to provide a non-reactive implant.

### 5.3. *Properties of the artificial heat source tested in vitro*

In order to study the surface temperature over the spherical heat source in a defined material, a Perspex<sup>(R)</sup> model, similar to the one described by Feasey, Davison and James (1971), was used. A heat source was placed between two Perspex<sup>(R)</sup> plates. The plate under the heat source (150 x 100 x 12 or 24 mm) was heated from the side opposite to the heat source by 37°C water. Perspex<sup>(R)</sup> plates of varying thickness, painted with Nextel<sup>(R)</sup> (3 M Comp.), could be stacked on the base plate and the heat source to allow "implant" depths of 3.3, 5.4, 6.6, and 9.7 mm. A surface temperature of about 30°C and a temperature gradient of about 3°C/10 mm was registered for the artificial model at an ambient temperature of 23 ± 0.1°C. The thermal and geometrical dimensions were similar to those of naked skin at calm (Hensel 1952).

The surface temperature over the heat source was studied in relation to the "implant" depth and the heat source power output.

It was obvious that the non-ideal physical situation, with a spherical heat source in a finite solid, influenced the temperature distribution. A calculation of the specific thermal conductivity of the surrounding Perspex<sup>(R)</sup> resulted in a mean value of 0.34 ± 0.02 W/m°C for the heat sources at depths of 5.4, 6.6 and 9.7 mm, whereas the most superficial implantation, at 3.3 mm, gave a conductivity of 0.4 W/m°C. A considerable variation in the conductivity value of acrylics is found in the literature, about 0.2 W/m°C being the most probable one for Perspex<sup>(R)</sup>. The variation in the measured conductivity as a function of the "implant" depth is due to the extension of the spherical heat source which introduces a deviation from the almost spherical isotherm of the point source theory. The mean value of 0.34 W/m°C, as compared to 0.2 W/m°C, can also be attributed to the finite test model. An increase of the base plate thickness from 12 to 24 mm resulted in a measured conductivity of about 0.3 W/m°C.

Experimental temperature profiles, registered over spherical heat sources in Perspex<sup>(R)</sup>, were in good agreement with the

corresponding theoretical calculations (Gustafsson, Nilsson and Torell 1974) of the temperature profile over a point heat source in an infinite homogeneous solid with a specific conductivity of  $0.3 \text{ W/m}^\circ\text{C}$ . The experimental and theoretical profiles for a specified power and depth are exemplified in Fig. 5.

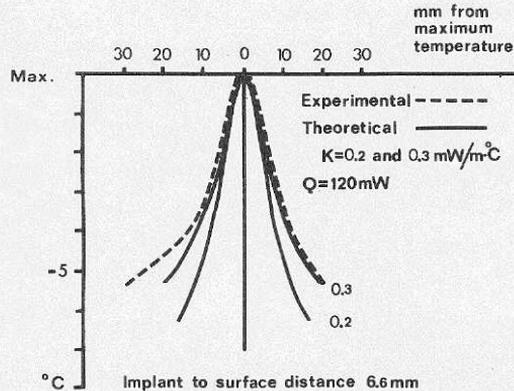


Fig. 5. Experimentally registered temperature profile over a  $120 \text{ mW}$  spherical heat source in a Perspex<sup>(R)</sup> plate at a distance of  $6.6 \text{ mm}$  from the surface, as compared to the corresponding theoretical profile over a point heat source in a material with a thermal conductivity of  $0.2$  and  $0.3 \text{ W/m}^\circ\text{C}$ .

The conclusion drawn from the in vitro test is that the non-ideal physical situation affects the temperature distribution as compared to the theoretical calculation. As could be expected, the influence is more pronounced for superficial "implantations". The results from heat sources at distances of more than  $5 \text{ mm}$  from the surface appear to be comparable.

#### 5.4. Experimental procedure with implanted heat sources

The heat sources were implanted subcutaneously in rabbits and man. In rabbits the heat sources were placed in the lower part of the abdominal wall (Paper I). In man the heat sources were placed in the lateral part of the upper arm (Paper III).

Implantation was performed under intravenous Nembutal<sup>(R)</sup> anesthesia in animals and under local anesthesia in humans.

A careful surgical procedure with specially designed introducers was used to avoid damage to the tissue during implantation. The loose subcutaneous tissue allowed blunt dissection and introduction of the heat sources.

In the initial animal experiments a short healing period (2-4 weeks) was allowed (Paper I), whereas further experiments with spherical heat sources in animals and man were performed after a healing period of 2-3 months (Paper III).

After the healing period the leads to the heat source were exposed through a skin incision at least 50 mm from the implant site and connected to the power supply and resistance measuring multimeter for temperature registration.

A detailed description of the measuring procedure is given in Paper III.

The principle of the measuring procedure was consistent for both animal and human experiments. The object was initially allowed to equilibrate to the ambient temperature for about half an hour. After this equilibration period the central heat source temperature, the skin temperature immediately over the heat source and the temperature distribution over a 55x65 mm area ( $35 \text{ cm}^2$ ) were registered for the zero-power heat source. The heat source was then activated by a DC voltage source connected to the heat coil leads. A 20 minutes' equilibration period was allowed in order to reach a semi-steady state for the power output from the heat source. After that the same registrations as for the initial zero power heat source were made. Repeated stepwise power increases were then performed, with corresponding registrations of heat source temperature and skin temperature.

In the experiments with heat sources implanted in man (Paper III) the ambient conditions were varied and the same procedure was repeated at forced convective heat loss from the skin surface (2 m/s,  $23^{\circ}\text{C}$ ) and at  $17^{\circ}\text{C}$  room temperature. The forced convection, i.e. the 2 m/sec wind, was blown over the skin with a fan and adjusted according to a wind speedometer (Wilh. Lambrecht 641 Z 0-5 m/s).

### 5.5. *Methods for measurement of the distance between the heat source and the skin surface*

In the animal experiments (Paper I) with button-like heat sources implanted in rabbits the distance between the heat source surface and the overlying skin was measured after rapid freezing in liquid nitrogen of the skin and tissue around the heat source in situ.

The spherical heat sources used for human experiments allowed roentgenological distance measurements from a tangential x-ray exposure over the skin area in question (Paper III). A marker was placed at the maximum temperature increase of the skin overlying the heat source during the IRT registration. The position of this marker was also checked by palpation and in perpendicular x-ray transillumination. The measured distance between the heat source and skin surface should at most exceed the real distance with 0.4 mm.

### 5.6. *Methods for definition of the tissue surrounding the heat sources.*

Conventional histologic specimens were taken from the tissue surrounding the heat sources implanted in animals in all cases. Htx-eosine staining was used. The histologic examination was aimed at characterization of the tissue surrounding the heat source and histologic signs of tissue injury reactions. In the human experiments histologic specimens were obtained in three cases.

In the animal experiments a microangiographic delineation of the vascular system was performed. The microangiography was performed immediately after the temperature distribution studies and in the same continuous anesthesia. The abdominal aorta was cannulated and barium contrast was infused after heparinization and vasodilation with lidocaine (Lundskog, Brånemark and Lindström 1968, Holm-Pedersen, Nilsson and Brånemark 1973).

After completed contrast infusion the skin and subcutaneous tissue with the heat source in situ was cut out. The specimen was then x-ray examined. For obvious reasons no microangiography could be performed on human implants.

The implantation area was carefully examined before the implantation, during the healing period and the experimental procedure, in order to register any clinical signs of adverse tissue reaction.

## 6. Theoretical analysis of the temperature distribution on the surface over a heat source

Draper and Boag (1971a) have given a theoretical description of the surface temperature distribution immediately over a point heat source in relation to the power, distance from the surface, thermal conductivity of the surrounding tissue, and the "surface thermal conductance".

In paper I this theoretical calculation was further developed in order to make possible manual calculation of the maximum temperature increase ( $\Delta T_0$ ) over a point heat source in relation to the mentioned four parameters:

$$\Delta T_0 = \frac{1}{2\pi K} \cdot Q \cdot \frac{1 + f(u)}{a}$$

This arithmetic calculation thus includes the heat source power (Q), the distance between the heat source centre and the skin surface (a), the thermal conductivity of the surrounding tissue (K), and the thermal conductance of the overlying surface (E).  $f(u)$  is a function of a, E and K ( $u = a \cdot E/K$ ) which can be expressed as an infinite series but has been put in tabular form for typical values of the three parameters.

A more detailed analytical description of the surface temperature distribution over a heat source has also been presented (Paper II).

Starting from the same general theoretical description of the temperature distribution around a point heat source in a homogeneous solid, at a certain distance from the surface and with specified thermal constants, a fairly simple expression can be deduced for the surface temperature profile over the heat source.

The calculations include the same four parameters as for the maximum temperature increase. The temperature profile is calculated with the maximum temperature as a reference.

The temperature decrease at a certain radius from this maximum temperature can be expressed as:

$$\Delta T(u, v) = \frac{Q \cdot E}{2 \pi K^2} \cdot I(u, v)$$

where Q, E, and u have been defined. v is defined as  $r \cdot E/k$ , r being the radius, for which the temperature decrease is to be calculated. I (u,v) is an integral that has been numerically evaluated and put in tabular form for typical values of a, E, K, and r.

With the results of the numerical integration available the temperature distribution over a defined point heat source in a homogeneous solid can be calculated and compared with experimental results and also to clinically registered temperature patterns.

## 7. Results and comments

In this summary the results are presented and discussed in relation to the aims of the work (Chapter 2).

### 7.1. *A theoretical description of the surface temperature distribution over a heat source in living tissue*

In accordance with the purposes of this study a method for calculation of the skin temperature over a heat source has been developed from the theoretical three-dimensional calculation of the temperature distribution around a point heat source (Paper I and II).

The equations presented make simple calculations of the maximum surface temperature possible as well as calculations of the temperature distribution of the surface overlying a heat source for specified values of heat source power, implant depth and of the surrounding tissue conductivity and overlying surface conductance. Tabulated integrals, necessary for the calculations, are given for adequate variations of these parameters.

As stated in Paper I, the theoretical results are presented with full awareness of the fact that no theoretical calculation, analytical or numerical, can account for the complex biological variations clinically registered or experimentally produced.

It is obvious, however, that theoretical work can delineate the dimensions of conductive heat distribution (Draper and Boag 1971b) and allow estimation of heat production (Gautherie, Bourjat, Quenneville and Gros 1972) in living tissues. "Artificial" test models may also be designed on the basis of theoretical considerations (Haberman, Francis and Love 1972).

### 7.2. *An experimental model for quantitative studies of the surface temperature distribution over a heat source in living tissue*

#### Surface temperature measurements

A surface temperature reference for experimental studies has been designed. A technique for calibration of the IRT instrument against this reference was developed.

An actual surface temperature measurement accuracy of  $\pm 0.2^{\circ}\text{C}$  was found for objects at the middle of the field of view and in the focal plane.

The influence of a small object size on the temperature measurement revealed a minimum circular object size of 3 mm in diameter and a minimum slit width of 2 mm for full temperature registration.

The influence of defocusing of varying object forms and dimensions was analysed. For the experimental conditions a focal depth of about  $\pm 5$  mm could be estimated, as no significant temperature decrease could be registered for the object forms or dimensions tested within this range.

A temperature accuracy of  $\pm 0.2^{\circ}\text{C}$  does not appear too impressive. As has been mentioned earlier, a temperature accuracy better than  $\pm 0.1^{\circ}\text{C}$  is claimed for many point radiometers and the same temperature accuracy of  $\pm 0.1^{\circ}\text{C}$  is claimed for scanning radiometers in most manufacturers' booklets as well as by several authors (Bowling Barnes 1968, Dodd, Zermeno, Marsh, Boyd and Wallace 1969, Gautherie, Jatteau, Ott and Quenneville 1972).

As a first step a series of model experiments was performed in order to characterize the IRT instrument (Nilsson 1970). As a result of this test, indicating the existence of considerable "machinery artifacts", several contact measuring techniques were tested for temperature registrations over heat sources "implanted" in artificial models and in rabbits.

The literature on surface temperature registration with different kinds of contact thermometers gives a variety of estimations of the accuracy achieved. The critical reports by Stoll and Hardy (1949, 1950) however, conclusively show the artifacts resulting from contact pressure on the local skin circulation as well as the influence of the environmental conditions.

The problems reported by these authors were confirmed and difficulties with high contact pressures necessary for stable registrations, the unpredictable effects on living objects with implanted heat sources just under the measuring point and also

difficulties in making a representative number of observations made us accept the thermal resolution of IRT. The "spatial" resolution of contact thermometry is obviously inferior to that of IRT. Considering the advanced mechanical and electronic treatment of the original radiation signal to be measured and the obvious "machinery artifacts" to be accounted for, claims of a temperature accuracy better than  $\pm 0.2^{\circ}\text{C}$  for IRT registrations of living objects appear at present to be unrealistic.

#### An implantable artificial heat source

Two versions of implantable heat sources have been used in the present study. A button-like 11x4 mm heat source was initially implanted in rabbits (Paper I). A modified, spherical heat source, with a diameter of 4.5 mm, was later designed and tested in vitro and implanted in rabbits and man (Paper III).

The requirements set up for the implantable heat source could be met. The power output could be registered and varied with an accuracy of 2% for a power output between zero and about 120 mW. The central heat source temperature could be registered with an accuracy of  $\pm 0.1^{\circ}\text{C}$ .

As judged from clinical, histological and angiographical registrations, the heat sources could be implanted without any untoward tissue reaction that could influence the heat distribution around the heat source. Clinically, the heat sources in animals and man healed without swelling, hyperemia, pain, or fibrosis.

The heat sources exposed after completed experiments were macroscopically surrounded by a slender capsule without inflammatory reactions. In man the heat source capsule appeared to be continuous with and of the same dimension as the thin connective tissue sheets dividing the subcutaneous fat lobuli.

Microscopically the encapsulation of the heat sources consisted of mature connective tissue. No microscopically detectable pathologic vessels could be seen.

Microangiograms of the animal heat sources revealed an increased vascularity corresponding to the encapsulation. If the thin capsule was dissected away, no abnormalities of the overlying skin vessels could be seen in the angiograms. It was quite obvious

however, that the normal overlying skin vessels, as registered with microangiography, in certain cases influenced the temperature distribution over the heat source (Paper I).

The very slight tissue reaction to the implant is a result of an atraumatic implantation procedure and a non-reactive implant material (Brånemark, Breine, Lindström, Adell, Hansson and Ohlsson 1969, Brettle 1970).

### Physical properties of the heat source

In biologic tissue heat production requires volume. This applies to both endogenous heat production and an experimental model with an artificial heat source. To allow a reasonable power output without producing a noxious local temperature increase, the heat must dissipate within a certain volume. A power output range from zero to 150 mW was estimated as adequate for the experimental model. The upper limit was calculated as the approximate maximum heat production from a sphere of living tissue with a radius of 10 mm and a specific heat production of  $25 \text{ mW/cm}^3$ . Empirically, an artificial spherical heat source with a radius of about 2.5 mm allowed a power output of 150 mW without giving rise to a central temperature exceeding  $45^\circ\text{C}$ .

These empirical results are valid for a heat source with the presented design, i.e. with a central thermistor and a heat coil cemented in epoxy (thermal conductivity  $0.2 \text{ W/m}^\circ\text{C}$ ) and encapsulated by a 0.5 mm titanium sphere (thermal conductivity  $22 \text{ W/m}^\circ\text{C}$ ).

The extent of the heat source necessarily affects the temperature distribution around it as compared to the ideal physical situation. The theoretical calculation of the surface temperature over a heat source is derived for a point source. However, the calculation should also give a good approximation of the surface temperature over a spherical heat source (Paper II). Spherical heat sources have been "implanted" in an artificial Perspex<sup>(R)</sup> model for an experimental illustration of how the non-ideal physical situation affects the overlying skin temperature distribution in relation to the theoretical calculation of the surface temperature distribution over a point heat source (Chapter 5.3).

As could be assumed "implantation" very close to the surface results in a more marked aberration than deeper "implantation". In vitro results indicate a critical implantation depth of about 5 mm. Thus, the results from more superficial implantations should not be directly compared to the results from deeper heat sources.

### *7.3. The skin temperature over the artificial heat source as a function of the heat source power and position*

#### Geometrical and thermal dimensions

Heat sources have been implanted in artificial models, in animals and in man. Two heat source designs have been used - an initial button-like one (4x11 mm) and a spherical one (diameter 4.5 mm).

The heat sources were implanted subcutaneously, at a distance from the centre of the heat source to the overlying skin surface of 3.2 - 7.9 mm in animals and 3.7 - 7.8 mm in man.

Heat source power outputs giving a maximum central heat source temperature of about 45°C are presented. The maximum skin temperature increase over the heat source appears to be almost linearly related to the power outputs.

The maximum skin temperature increase over the superficial heat sources naturally exceeds the temperature increase for the corresponding power outputs from deeper heat sources. However, no strict relation between implant depth and skin temperature increase was found in animal experiments or with heat sources implanted in man.

The results from the heat sources implanted in man can be used to illustrate the geometrical and thermal dimensions studied (Paper III). A heat source power output of 10 mW was necessary to provoke a 0.5°C surface temperature increase over the heat source at a distance of 3.7 mm from the skin surface. A power output of about 25 mW was necessary from the heat source at a distance of 7.8 mm for the same 0.5°C temperature increase. For a 1°C surface temperature increase a power output of about 15 mW was necessary from the superficial heat source, the corresponding value for the deeper heat source being about 40 mW.

A central heat source temperature of  $37^{\circ}\text{C}$  - which represented a temperature increase of  $6^{\circ}\text{C}$  in relation to the zero power temperature - was achieved at a heat source power of about 50 mW. This central temperature resulted in a  $3^{\circ}\text{C}$  and a  $1.5^{\circ}\text{C}$  surface temperature increase over the 3.7 mm and 7.8 mm heat source, respectively.

### Calculation of thermal conductivity

The relation between heat source power output, implant depth and the resulting skin temperature increase can be used in a theoretical calculation of the thermal conductivity of the tissue surrounding the heat source (Paper I).

The thermal conductivity resulting from such a calculation must be regarded as a mean effective thermal conductivity of the tissues around the heat source. In the animal experiments this implies that the resulting conductivity includes mainly skin and underlying muscles. In experiments with heat sources implanted in humans the subcutaneous fat also affects the temperature distribution.

The thermal conductivity calculated from the experimental measurements with button-like heat sources implanted in animals was  $0.9 \text{ W/m}^{\circ}\text{C}$ . Unpublished results from measurements with spherical heat sources implanted in animals gave a calculated thermal conductivity of  $0.6 \pm 0.1 \text{ W/m}^{\circ}\text{C}$ . This difference could probably be attributed to the asymmetric form and heat dissipation of the original heat source.

The thermal conductivity calculated from the experimental measurements with heat sources implanted in man gave values ranging from 0.4 to  $0.7 \text{ W/m}^{\circ}\text{C}$  with a mean value of  $0.52 \pm 0.12$ .

These experimental results should be compared to the values of the thermal conductivity of living tissues reported in the literature and summarized in Chapter 3.1.

The conductivity of fat is fairly constant, about  $0.2 - 0.3 \text{ W/m}^{\circ}\text{C}$ , whereas the values of the conductivity of muscular tissue and skin vary considerably, from about  $0.4 \text{ W/m}^{\circ}\text{C}$  to  $0.8 \text{ W/m}^{\circ}\text{C}$ . Of course, this variation is an expression of the difficulties involved in measuring under standardized conditions and also of the fact that the values represent effective thermal conductivity, including specific conductivity and convection with blood.

One of the major functions of the skin is to execute the intentions of the thermoregulatory centre by varying its effective thermal conductivity, i.e. actually varying the convective heat transport through the skin. In vivo measurements of the effective skin conductivity must reflect this function. Measurements of the effective conductivity of skin are also complicated by the local effect of heat on skin circulation (Hensel 1952, Hertzman 1961). Values for non-perfused skin conductivity ranging from 0.4 to 0.6 W/m<sup>0</sup>C have been reported, the value for skin in the comfort zone (undressed at about 27<sup>0</sup>C) probably not being considerably higher. Vasodilatation achieved by local heating, on the other hand, may provoke a three to fourfold increase of the effective thermal conductivity (Lipkin and Hardy 1954). The increase is most likely to take place in the deeper, more vascularized layers of the skin (Hensel 1952). In our experimental studies in animals (Paper I) and man (Paper III), however, a linear relation was found between the power output from the implanted heat source and the overlying surface temperature increase. This was a constant finding, indicating that the local heating effect of the heat source power outputs presented did not provoke any registrable change in the effective thermal conductivity of the surrounding tissue.

#### Surface temperature distribution

The complete temperature distribution of the skin overlying the heat sources in relation to heat source power output and implantation depth has been presented as temperature profiles over button-like heat sources in rabbits (Paper I) and spherical heat sources implanted in man (Paper III).

The temperature profiles over heat sources implanted in biologic tissues are influenced by the fact that the skin over the zero power heat source does not display an even temperature but an arbitrarily distributed temperature gradient. A temperature gradient of up to 2<sup>0</sup>C has been registered in the animal experiments over the field of view (65 x 55 mm). The human skin appeared to be more homogeneous, with a corresponding temperature gradient of 0.5 to 1<sup>0</sup>C.

Because of this perturbed background, the temperature profiles cannot be directly correlated to the ideal physical situation with an initially even surface temperature. For a comparison between the experimental and theoretical temperature profiles the temperature decrease from the maximum temperature has been used (Papers II and III). This means that the maximum skin temperature over the heat source has been used as a reference temperature and the successive temperature decrease at an increasing radius from this point plotted. A comparison between experimental results from a power output of 120 mW from heat sources implanted at varying depths in man and the corresponding theoretical calculation reveals a reasonably good correlation (paper III). The temperature profiles from the experimental results appear to be wider than the theoretical equivalent, which could be expected from a non-point source.

#### *7.4. The influence of varying environmental conditions on the skin temperature distribution over the heat source*

The influence of forced convection (a 2 m/s air stream) and lowered ambient temperature (17°C) was studied for heat sources implanted in man (paper III).

##### Forced convective heat loss

A consistent finding was that a forced convective heat loss resulted in a considerably lowered zero-power heat source temperature and skin temperature over the heat source. The registered surface temperature increase immediately over the heat source in relation to the power output was also considerably smaller. The measured values of the surface temperature increase immediately over the heat sources at forced convection were about 40%, 50% and 60% of the initial values at power outputs of 30 mW, 70 mW and 120 mW, respectively.

The width at half-height for comparable temperature profiles was in all registrations less in the forced convection series (25 - 60% of the initial values).

The experimental results are qualitatively consistent with the theoretical calculations presented by Draper and Boag

(1971b) and Feasey, Davison and James (1971). The temperature contrast reduction is, however, more pronounced than could be expected from theoretical considerations.

The cooling of the tissue should result in a decreased skin circulation and thus in a decreased effective conductivity. Such a physiologic change should counteract the physical effect of the forced convection.

The temperature increase over the heat source at a specified central heat source temperature (e.g. 37°C) shows that about 80% of the temperature increase at wind still is registered at forced convection, which is in good agreement with data on line sources presented by Draper and Boag (1971b).

The statement by Feasey, Davison and James (1971) that forced cooling will decrease the temperature contrast over a constant power source is thus strengthened by the present experimental results. The same authors indicate a possibility to increase the thermal contrast of superficial constant-temperature sources by moderate cooling. From theoretical considerations, however, the risk of overcooling is stressed.

#### Lowered ambient temperature

A decrease of the room temperature from 23°C to 17°C caused about the same central zero-power heat source temperature decrease and skin surface temperature decrease as the forced convection at 23°C.

No change in the relation between the measured heat source power output and the maximum skin temperature increase could be registered, i.e. the temperature contrast over a constant power source was not increased.

If, on the other hand, the heat source was regarded as a constant temperature source (central heat source temperature 37°C), this resulted in a temperature increase over the heat source that was about 40% higher. These experimental results indicate that a moderate cooling rate increases the temperature contrast. It should be emphasized that the increased surface temperature was due to a parallel power and central heat source temperature increase.

## 8. Summarizing remarks on heat production and heat distribution in living tissues and in the experimental model

### 8.1. Heat production

The metabolic process in a living tissue is an exothermic reaction. The rate of heat production from this reaction naturally varies. The range of this variation in normal tissues can be illustrated by the low heat production from fat tissue of about  $0.5 \text{ mW/cm}^3$  and the maximum values reported for kidney cortex of  $30 \text{ mW/cm}^3$ . These values are calculated from the oxygen consumption of the tissue in question (Draper and Boag 1971b).

In spite of an enormous interest in tumour metabolism from a chemical point of view, very sparse information concerning the heat production in neoplastic tissues is available. As for normal tissue, the metabolic heat production of a malignant tissue can be calculated from the oxygen consumption of tissue cultures. Draper and Boag (1971b) have given values of the possible metabolic heat production in various normal tissues and clinical and experimental tumours. The calculations were based on the oxygen consumption or carbon dioxide production of the respective tissues (Roskelly, Mayer, Horwitt and Salter 1943, Both, Boyland and Cooling 1967). The possible heat production calculated for some normal and pathologic tissues is presented in Table 1. In the same table the approximate perfusion rate (Folkow, Neil 1971) for the normal tissues is given. The values have been converted from the dimension  $\text{ml}/100\text{g}\cdot\text{min}$  to  $\text{ml}/\text{cm}^3\cdot\text{sec}$  in order to facilitate a comparison with the heat transport capacity of the circulation.

Gautherie, Bourjat, Quenneville and Gros (1972) have described a method directly aimed at measuring the specific heat production of tumours in situ. A specific heat production of between  $1.7$  and  $49 \text{ mW/cm}^3$  was found for eight mammary cancers. This value includes metabolic and circulatory contributions to the heat production.

The magnitude of the circulatory "contribution" to the local heat production is open to discussion. Theoretically, the

Table 1. Calculated metabolic heat production rates for various normal and pathologic tissues (Draper and Boag 1971b) and corresponding blood flow during rest (Folkow and Neil 1971).

Tissue	Metabolic heat production $\text{mW}/\text{cm}^3$	Blood flow <sub>3</sub> during rest $\text{ml}/\text{cm}^3 \cdot \text{sec}$
Skin	2.5 - 5	$1.6 \cdot 10^{-3}$
Liver	2.8	$14 \cdot 10^{-3}$
Kidney	11	$66 \cdot 10^{-3}$
Ca. various	2.5 - 13	?
Cystic mastitis	5.8	?

heat power supplied to a certain tissue volume can be calculated from the blood perfusion rate and the temperature fall between the supplying and draining blood vessels (Tregear 1966).

To illustrate the magnitude of such a circulatory contribution, a temperature fall of  $1^{\circ}\text{C}$  can be arbitrarily chosen for estimation of the heat released per  $\text{cm}^3$  tissue at various flow rates (Table 1). Assuming a flow rate corresponding to that registered for kidneys - about  $400 \text{ ml}/\text{min} \cdot 100\text{g}$  corresponding to about  $66 \cdot 10^{-3} \text{ ml}/\text{cm}^3 \cdot \text{sec}$  - a temperature fall of one centigrade between the afferent and efferent vessels should give a heat output of almost  $300 \text{ mW}/\text{cm}^3$ ! The modest flow rate of resting muscle or fat should produce a heat output of  $2 \text{ mW}/\text{cm}^3$ .

According to Lawson and Chughtai (1963) the effect of the vascular system with respect to the local energy balance is inverse to these calculations. The temperature of the venous drainage from breasts with malignant tumours was found to be about  $1^{\circ}\text{C}$  higher than that of the arterial supply. Direct intratumoral temperature measurements showed the temperature to be another centigrade higher. From these results the authors conclude that the vascular flow actually drains the increased metabolic heat production. The experimental conditions are not reported in details and the interpretation of the results has been questioned.

It thus appears difficult to give a quantitative value for the specific heat production of a circumscribed tissue volume, whether mainly metabolic, metabolic and circulatory or mainly

circulatory. A calculation of the total heat production within a spherical tissue volume of increasing radius, a specific heat production of  $25 \text{ mW/cm}^3$  being assumed, has been presented (Paper I). An extension of this calculation to include other values of specific heat production is presented in Fig. 6a, where the total heat production from spheres of increasing radii has been plotted for specific heat productions of 10, 25 and  $50 \text{ mW/cm}^3$  (continuous lines).

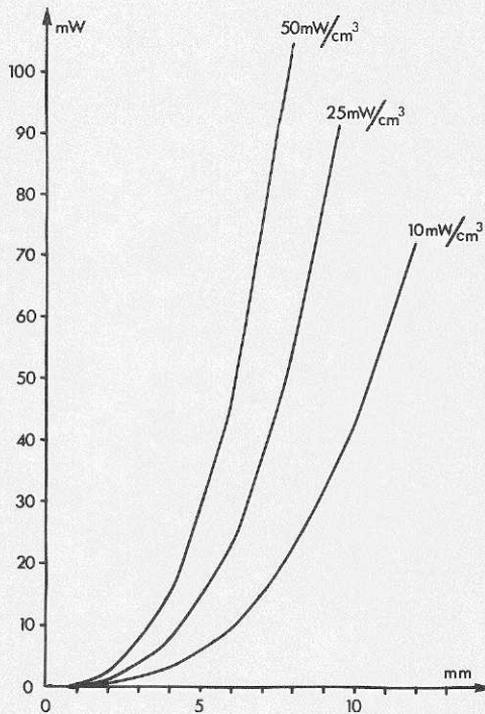


Fig. 6.a. Theoretical calculation of the possible heat production (ordinate) from a spherical tissue volume of increasing radius (abscissa). The calculation has been performed for three values of specific heat production ( $10$ ,  $25$ , and  $50 \text{ mW/cm}^3$ ).

A specific heat production of  $25 \text{ mW/cm}^3$  should limit the possible power output from the spherical experimental heat source to just above 1 mW! The approximate power values for the same sphere with a 2.5 mm radius at a specific heat production of 10 or  $50 \text{ mW/cm}^3$  can be estimated from the diagram.

## 8.2. Heat distribution

For definite values of the thermal conductivity of the tissue, the temperature distribution around a heat source in a living tissue as well as the temperature distribution of the overlying skin surface can be calculated (Draper and Boag 1971a,b, Nilsson and Gustafsson 1974, Gustafsson, Nilsson and Torell 1974).

It is possible, e.g., to estimate the approximate power output from a heat source necessary to provoke a certain temperature increase on the overlying surface. In Fig. 6b the power output from a point heat source that should result in a  $0.5^{\circ}\text{C}$  temperature increase of the overlying surface is shown for heat sources at various depths and for various tissue conductivities (interrupted lines).

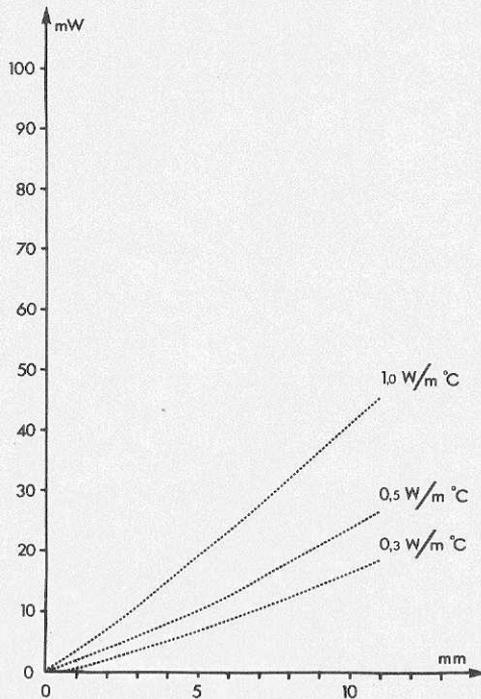


Fig. 6.b. Theoretical calculation of the heat production (ordinate) from a point heat source at increasing distance from the skin surface (abscissa), which should result in a  $0.5^{\circ}\text{C}$  surface temperature increase immediately over the heat source. The calculation has been performed for three values of thermal conductivity of the surrounding tissue ( $0.3$ ,  $0.5$ , and  $1.0 \text{ W/m}^{\circ}\text{C}$ ).

The two diagrams can be combined in order to illustrate the relation between the possibility of metabolic heat production in living tissues and the heat production necessary to provoke even a minor local temperature increase at the surface over a heat source (Fig. 6c).

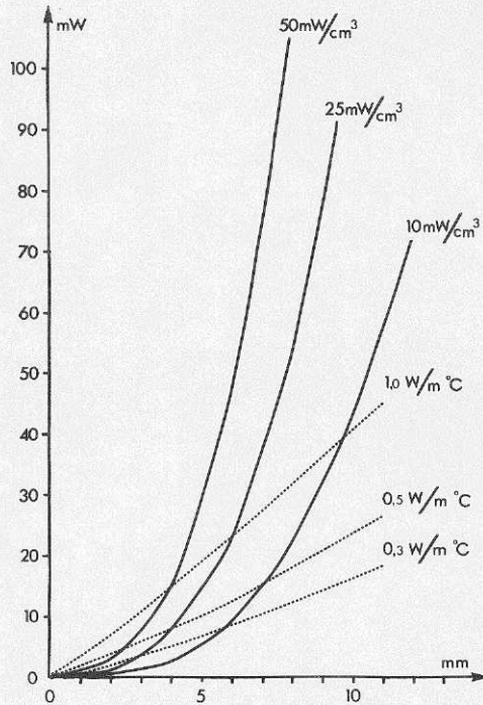


Fig. 6.c. Combination of Fig. 6.a and 6.b to give a theoretical illustration of the relation between possible (6.a, continuous lines) and necessary (6.b, interrupted lines) heat production from a buried heat source, resulting in a detectable surface temperature increase.

Theoretical calculations and consonant experimental results indicate the limitations of metabolic heat production and conductive heat distribution as an origin for localized skin temperature changes.

For breast tumour diagnosis, clinical experience has given the same conclusion: the original simple "hot spot" diagnosis must be replaced by more complex diagnostic criteria. The vascular reactions, as reflected in the subcutaneous veins, probably constitute one of the most important parameters for

the evaluation of breast thermograms (Freundlich, Wallace and Dodd 1968, Dodd, Zermeno, Marsh, Boyd and Wallace 1969, Draper and Jones 1969, Lapayowker, Kundel and Ziskin 1971, Barash, Pasternack, Venet and Wolff 1973).

The conception of thermography as a method closely related to circulatory changes indicates the wide range of other applications where circulatory changes in superficial tissues are primary, e.g. septic and aseptic inflammations, burns, skin disorders, and peripheral vascular disturbances of various etiologies. The use of thermography as a diagnostic method in these fields, as well as in breast cancer diagnosis, rests to a large extent on the vascular reactions in superficial tissues.

## 9. Summary and conclusions

The conclusions of the theoretical and experimental work are presented according to the aims of the investigation (Chapter 2).

1. The analytical description of the three-dimensional heat distribution around a heat source was developed to give an arithmetic expression of the surface temperature over the heat source as a function of:
  - the power output of the heat source
  - the thermal conductivity of the surrounding tissue
  - the surface conductance
  - the distance between the heat source and the surface
  - an integral of the last three parameters given in tabular form

Theoretical calculations can delineate the dimensions of heat production and conduction in a tissue as a basis for a discussion of the mechanisms underlying localized skin temperature changes registered over, e.g., breast tumours, inflammatory reactions and vascular disturbances.

2. An experimental model for quantitative studies of the skin temperature distribution over an artificial heat source implanted in animals and man was developed. The method includes:
  - a skin temperature measuring technique using infrared thermography with a thermal resolution capacity of  $\pm 0.2^{\circ}\text{C}$  and a spatial resolution of  $\pm 1$  mm.
  - an implantable heat source with adjustable and registrable power output and central temperature.
  - a method for atraumatic implantation of heat sources in animals and man. Heat sources have been implanted without tissue reactions that could affect the local heat distribution.

3. The experimental model has been used for studies of the skin temperature distribution in relation to the heat source power output and the distance between the heat source and the skin surface studied.

The experimental results demonstrate that high power output or close-to-surface position is necessary to provoke a registrable surface temperature increase.

4. Forced convective heat loss from the surface studied results in a decreased temperature contrast over the heat source, whether regarded as a constant-power source or as a constant-temperature source.

No obvious change in temperature contrast over the heat source was registered over a constant-power source at 17 °C as compared to an ambient temperature of 23 °C. An increased temperature was registered over a constant-temperature source at lowered ambient temperature.

5. Localized skin temperature changes can only in exceptional cases be attributed to conduction of metabolic heat produced in a circumscribed tissue underlying the surface.

An implicit conclusion of this statement is that such changes are due to other mechanisms, directed convective heat transport in superficial vessels probably constituting the most important pathway.

## REFERENCES

- BARASH, I.M., PASTERNAK, B.S., VENET, L. and WOLFF, W.I., 1973, *Cancer*, 31, 769.
- BOOTH, J., BOYLAND, E. and COOLING, C., 1967, *Biochem. Pharmacol.*, 16, 721.
- BOWLING BARNES, R., 1968, *Applied Optics*, 7, 1673.
- BRETTLE, J., 1970, *Injury*, 2, 26.
- BRÅNEMARK, P-I., BREINE, U., LINDSTRÖM, J., ADELL, R., HANSSON, B.O. and OHLSSON, Å., 1969, *Scand. J. Plast. Reconstr. Surg.*, 3, 8.
- BRÅNEMARK, P-I. and NILSSON, S.K., 1969, *Bibl. Radiol.* 5, 130.
- BURTON, A.C., 1948, *Methods in Medical Research* 1, 146.
- CHARLES, J.A. and FRANCIS, J.E., 1973, *Rev. Sci. Instr.*, 44, 291.
- COBET, R. and BRAMIGK, F., 1924, *Deutsches Arch. Klin. Med.*, 144, 45.
- COOPER, T., RANDALL, W.C. and HERTZMAN, A.R., 1959, *J. Appl. Phys.*, 14, 207.
- DODD, G.D., ZERMENO, A., MARSH, L., BOYD, D. and WALLACE, J.D., 1969, *Cancer*, 24, 1212.
- DRAPER, J.W. and JONES, C.H., 1969, *Br. J. Radiol.*, 42, 401.
- DRAPER, J.W. and BOAG, J.W., 1971a, *Phys. Med. Biol.*, 16, 201.
- DRAPER, J.W. and BOAG, J.W., 1971b, *Phys. Med. Biol.*, 16, 645.
- ELAM, R., GOODWIN, D.W. and LLOYD-WILLIAMS, K., 1963, *Nature*, 198, 1001.
- FEASEY, C.M., DAVISON, M. and JAMES, W.B., 1971, *Phys. Med. Biol.*, 16, 213.
- FELDMAN, F., 1969, *Cancer*, 23, 803.
- FOGED, J., 1932, *Scand. Arch. Physiol.*, 64, 251.
- FOLKOW, B. and NEIL, E., 1971, *Circulation*, Oxford Univ. Press, London.
- FREUNDLICH, I.M., WALLACE, J.D. and DODD, G.D., 1968, *Am. J. Roentgenology*, 102, 927.
- GAUTHERIE, M., BOURJAT, P., QUENNEVILLE, Y. and GROS, C.H., 1972, *Rev. Eur. Etud. Biol.*, 17, 776.
- GAUTHERIE, M., JATTEAU, M., OTT, J. and QUENNEVILLE, Y., 1972, *Path. Biol.*, 20, 559.
- GERSHON-COHEN, J., HABERMAN, J.A.D. and BRUESCHKE, E.E., 1965, *Radiol. Clin. of North Am.*, 3, 403.
- GUSTAFSSON, S.E., NILSSON, S.K. and TORELL, L., 1974, *Phys. Med. Biol.*, Accepted for publication.

- HABERMAN, J.A.D., FRANCIS, J.E. and LOVE, T.J., 1972, *Radiology*, 102, 341.
- HALL, W.M., 1973, *Jet. Prop. Lab. Space Progr. Sum.*, 4, 108.
- HAMMEL, H.T., 1968, *Ann. Rev. Physiol.*, 30, 641.
- HARDY, J.D., 1934a, *J. Clin. Invest.*, 13, 593.
- HARDY, J.D., 1934b, *J. Clin. Invest.*, 13, 605.
- HARDY, J.D., 1934c, *J. Clin. Invest.*, 13, 615.
- HARDY, J.D. and MUSCHENHEIM, C., 1934, *J. Clin. Invest.*, 13, 817
- HARDY, J.D. and MUSCHENHEIM, C., 1936, *J. Clin. Invest.*, 15, 1.
- HARDY, J.D., 1939, *Am. J. Physiol.*, 127, 454.
- HARDY, J.D., HAMMEL, H.T. and MURGATROYD, D., 1956, *J. Appl. Phys.*, 9, 257.
- HENRIQUES, F.C. and MORITZ, A.R., 1947, *Am. J. Path.*, 23, 531.
- HENSEL, H., 1952, *Ergebnisse der Physiologie*, 47, 166.
- HERTZMAN, A.B., 1961, *Adv. Biol. Skin*, 2, 98.
- HOLM-PEDERSEN, P., NILSSON, K. and BRÅNEMARK, P-I., 1973, *Adv. Microcirc.*, 5, 80.
- HONMA, K., KIMURA, K., HARADA, E. and SEKINE, K., 1966, *Zeitschrift für Biologie*, 115, 287.
- KALLIOMÄKI, K. and WALLIN, P., 1971, *J. Sci. Instr.*, 7, 535.
- LAPAYOWKER, M.S., KUNDEL, H.L. and ZISKIN, M., 1971, *Cancer*, 27, 819.
- LAWSON, R.N., 1956, *Canad. M. A. J.*, 75, 309.
- LAWSON, R.N. and CHUGHTAI, M.S., 1963, *Canad. M. A. J.*, 88, 68.
- LEIDEN, 1969, *Medical thermography. Bibl. Radiol.*, 5, 1.
- LIPKIN, M. and HARDY, J.D., 1954, *J. Appl. Physiol.*, 7, 212.
- LEWIS, D.W., GOLLER, H.O. and TEATES, C.D., 1973, *Diagn. Radiol.*, 106, 95.
- LUNDSKOG, J., BRÅNEMARK, P-I. and LINDSTRÖM, J., 1968, *Adv. Microcirc.*, 1, 152.
- MACEY, D.J. and OLIVER, R., 1972, *Phys. Med. Biol.*, 17, 563.
- MASSOPUST, L.C., 1948, *Surg. Gyn. Obst.*, 86, 54.
- MASSOPUST, L.C. and GARDNER, W.D., 1950, *Surg. Gyn. Obst.*, 91, 717.
- MAXWELL-CADE, C., 1968, *Radiography*, 34, 23.
- MITCHELL, D., WYNDHAM, C.H., HODGSON, T. and NABARRO, F.R.N., 1967, *Phys. Med. Biol.*, 12, 359.
- NEW YORK, 1964. *Thermography and its clinical applications. Ann.N.Y.Acad. Sci.*, 121, 1.

- NILSSON, S.K., 1970, *Adv. Microcirc.*, 3, 67.
- NILSSON, S.K. and GUSTAFSSON, S.E., 1974, *Phys. Med. Biol.*, 19, Nr.5,  
In press.
- ROSKELLY, R.C., MAYER, N., HORWITT, B.N. and SALTER, W.T., 1943, *J. Clin. Invest.*, 22, 743.
- STEKETEE, J., 1973, *Phys. Med. Biol.*, 18, 686.
- STOLL, A.M. and HARDY, J.D., 1949, *Rev. Sci. Instr.*, 20, 678.
- STOLL, A.M. and HARDY, J.D., 1950, *J. Appl. Phys.*, 2, 531.
- STOLL, A.M., 1960, *J. Heat Transf.*, 82, 239.
- STOLL, A.M., 1964, *Ann. N.Y. Acad. Sci.*, 121, 49.
- STRASSBOURG, 1967. *Colloque international de thermographie médicale.*  
*J. Radiol. Electrol.*, 48, 1.
- TABERN, D.L., KEARNEY, J. and DOLBOW, A., 1966, *Surgery*, 60, 1058.
- TREGGAR, R.T., 1966, *Physical Functions of Skin.* Acad. Press, London.
- WATMOUGH, D.J. and OLIVER, R., 1968a, *Nature*, 218, 885.
- WATMOUGH, D.J. and OLIVER, R., 1968b, *Nature*, 219, 622
- WATMOUGH, D.J. and OLIVER, R., 1969, *Br. J. Radiol.*, 42, 411.
- WATMOUGH, D.J., FOWLER, P.W. and OLIVER, R., 1970, *Phys. Med. Biol.*, 15, 1.
- WOLFE, W.L., 1964, *Ann. N.Y. Acad. Sci.*, 121, 57
- YOUNG, G.B., 1970, *Crit. Rev. Radiol. Sci.*, 1, 593.

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