Contribution of infrared thermography to the surveillance of irradiated breast carcinomas

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SUMMARY. The effect of ionising radiation on the metabolic heat production by cancers was investigated on a group of 31 small breast carcinomas (Tl and T2), all treated exclusively by radiotherapy under equivalent conditions (““Co) and then followed up regularly (mean recall period five years). The following techniques were used: (a) intratumoral thermometry and fluvography to compute the specific heat power of the tumour, (b) infra-red thermography for analysing the skin thermal pattern quantitatively. In particular, comparison of clinical, radiographic and thermal findings has shown: (a) constant agreement between the final loco-regional results of radiotherapy and the evolution of both the metabolic heat production by the tumor and the related hyperthermia on the skin; (b) the early appearance of the thermal signs of either a regression or a recurrence of the tumour, compared with the corresponding morphological signs. The fundamental and practical consequences can be summarised as follows: (1) distinction between radiosensitive and radioresistant carcinomas according as the specific heat power of the tumour is reduced or not after irradiation; (2) the definition of three types of thermal evolution characterized by normalisation, regression followed by re - increase, or continuance of both tumor heat production and malignant skin hyperthermia, and corresponding to the clinical concepts of sterilisation, recurrence and non-sterilisation, respectively; (3) justification of the systematic use of thermal methods for post-irradiation follow-up, especially to detect a local recurrence earlier and to specify the nature of any doubtful remaining opacity; (4) description of objective thermal criteria enabling a decision regarding a' repair mastectomy to be taken at **an earlier moment.**

Key words: breast cancer; metabolic heat production; post-irradiation follow-up; thermography; radiotherapy (““Co).

INTRODUCTION

In previous works [9,11] we showed that the growth and heat production of breast carcinomas are two typical and dependent phenomena. More particularly, the metabolic heat generated by the tumour per units volume and time is inversely proportional to its doubling time, the two parameters being constant for any particular cancer during the growth phase when growth is assumed to be exponential. This result proved extremely important because it provides an original and objective means of establishing a pre-therapeutic prognosis of small carcinomas either by determining the specific heat production by means of intratumoral thermometry and thermofluvography, or by the analysis of cutaneous hyperthermia by means of infra-red or liquid crystals thermography.

Non-mutilating therapy of breast carcinomas acts on the growth of the tumour and consequently on its thermicity, as we observed after various additive hormonotherapies (7). The purpose of the present paper is to analyse, using the same methods and strict confrontations with clinical and radiographic data, the effects of radiotherapy on metabolic heat production. This subpects is interesting under

Research supported by the French National Institute for Health and Medical Research (I.N.S.E.R.M) contracts nr. 71.1.014 and 73.1.008. The present work is an up-to-date version of a similar one already issued in french (GAUTHERIE et al., 1975 c); especially the results reported on figure 4 concern a higher number of cases.

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two heads: (a) on the fundamental level of radiopathology because our knowledge of the thermal consequences of irradiation needs still to be improved; (b) from the practical point of view of post-radiotherapic follow-up since the methods at present available are recognised as insufficient.

Apart from various difficulties of an experimental nature which have already been stressed in previous articles [8,9], a study of this kind requires a high number of cases and a long recall period in order to have statistical significance. Although apparently not very exacting, these requirements in fact mean that the Senology Department in charge has to possess certain characteristics which are rarely found in combination, namely: (a) a very large number of consultants so that even when the pathological classification is very detailed a statistically significant number of cases can be maintained; (b) ,a single medical responsibility extending through all the diagnostic and therapeutic stages and authorising the collection of the results of successive examinations from the first consultation to the checks several years after the treatment; (c) a rich arsenal of complementary investigation methods, microscopic and macroscopic, morphological and dynamic, ensuring a more complete and more subtle approach to the problems of diagnosis and surveillance.

PATIENTS AND METHODS

The various methodological problems having been discussed in detail in the preceding two articles [8,9], we will confine our observations on this subject to describing certain specific aspects of the present work, chiefly concerning the selection of patients and the experimental procedures.

SELECTION OF PATIENTS AND FOLLOW-UP

The investigation concerns 31 patients aged between 34 and 68 suffering from breast cancer (Tl or T2). All were treated by irradiation solely (^{60}Co), then regularly checked. Only cases treated before 1971 were considered in order to ensure sufficient distance in time to appreciate the effects of treatment. The irradiation was conducted in accordance with the recently redefined principles [3] and under practically equivalent conditions. Despite the differences in the procedures adopted, particularly with regard to the chronology of the treatments, we were able to verify a posteriori that the TDF factor (Time-Dose-Fractionation factor defined by Orton and Ellis [4, 17]) was between 145 and 160 in all cases. The post-irradiation surveillance consisted in clinical, radiographic and thermographic checks carried out systematically 1, 3, 6, 12, 18 and 24 months after the end of the course of treatment, then annually.

Since the method for evaluating heat production applies only to small, shallow and clearly defined carcinomas, the patients were selected on the basis of these technical criteria. The fact that these cancers are generally operated upon and not irradiated explains the relatively low number of cases studied compared with the number of cancers irradiated annually (nearly 200). Because of the fairly long time required for intramammary thermofluvographic measurements, the latter were ‘carried out only three times in order‘to spare the patient: (1) before treatment, (2) about 6 months afterwards, (3) then between 2 and 3 years later, depending on the general evolution of the carcinoma. Since the observations covered a period of several years, we paid particular care to the calibration of instruments, the stability of the thermal environment, and also the chronological similarity of the measurements in order to limit the influence of the circadian rhythm and the menstrual cycle. Despite these precautions, certain series of measurements were finally disregarded because they were incomplete or non-significant (repair surgery within a short period after irradiation, time schedule of checks not adhered to,. . .).

THERMAL INVESTIGATIONS

Analysis of the temperature distribution over the breast was carried out by infrared thermography and in some cases by liquid crystals thermography in constant-temperature (21+ l°C) and draught-free conditions and after a 10 mn-period of acclimatization to the thermal environment (spontaneous cooling). In each case, we made: (a) a qualitative analysis of the thermal pattern by recording pictures of each breast and << centred >> pic-

tures of the cancer breast especially to determine the topography of the vascular hyperthermia; (b) a quantitative analysis by measuring temperatures differences and gradients, especially by means of the isotherm and thermal profile functions of the infrared camera previously calibrated with respect to two reference black bodies.

Simultaneous measurements of temperature (thermometry) and thermal conductivity (fluvography) were made with the aid of sterile needle probes implanted in the breast after local anaesthetic, first on the cancerous side, then on the normal side in symmetrical regions and directions. On the cancerous side, the implantation, guided by palpation and checked by radiographic means was such that the needle passed through the tumor nearly at its centre. The measurements were made at intervals of about 5 mm, beginning at the maximum depth of implantation (the same as the length of the needle or 65 mm). We should point out that, though technically difficult, these measures, if elementary precautions are taken, are free from danger, not painful and readily accepted by the patient.

Computer calculation of the specific heat-producing power q* of the cancer was effected using the following formula previously arrived at on the basis of physical and mathematical models:

$$q^{\star} = \frac{12\,\Delta T_Y}{D^3}\left[\int_0^{\infty} \frac{\lambda \cdot \exp\left[-\lambda\,(Y+P)\right]}{h + k_e \cdot \lambda} \cdot d\lambda - \frac{P}{k_e\,(P^2 - Y^2)}\right]^{-1}$$

q* (W/cm^3) =specific heat power, i.e. the quantity of heat produced per unit of volume of the tumour and per unit of time.

D, P (cm) = diameter and depth of the tumour, as measured on the radiograph (allowance being made for the enlargement).

AT, (°C)= difference between the temperature measured at the circumference of the tumour at the nearest point to the skin, called Y (cm), and the temperature at the symmetrical point in the normal breast.

k_e (W/cm "C) = thermal conductivity of the breast tissue at point Y measured by fluvographs.

h (W/cm^2 °C) = overall coefficient of heat exchange by radiation, convection and evaporation between the surface of the skin and the surroundings, assumed to be constant and equal to $1.10^{-3} W/cm^2$ °C, for the thermally controlled conditions in which the measurements were made.

The physiopathological significance of the thermal conductivity (function of tissular blood flow) and of the specific heat power of the cancer tissue, has been discussed in a previous paper [8].

RELIABILITY OF MEASUREMENTS

The dynamic study of a phenomenon demands above all that the measurements should be reproducible, a condition guaranteed principally by stability of the equipment used and the consistency of the experimental conditions. This last requirement is very difficult to satisfy in the case of biological material, more particularly of patients, and when the measurements are discontinuous and carried out at intervals of weeks or even months. We therefore frequently checked the calibration of our instruments, particularly the fluvograph, and carried out the measurements in the same thermal environment (room temperature stabilized at 21°& l°C), at the same time of day (middle of the afternoon) and at the same (post-menstrual) phase of the menstrual cycle in the case of patients who had not reached the menopause. The observation of this last condition is important because the passage of blood through the breast tissue and, consequently, the effective thermal conductivity of the breast tissue as measured fluvographically, increases appreciably during ovulation. Furthermore, during the first series of measurements, photographs and radiographs were made in order to (re) locate as accurately as possible the position of the patient and of each breast and, more especially, the site and direction of implantation of the fluvographic needle probe. The measurements which followed were only considered significant if the needle passed through the tumour in approximately the same direction at the first time.

ANALYSIS OF DATA

The thermal and morphological evolution after irradiation were represented graphically

for each patient considering three categories of variables:

Intramammary thermal parameters. At the three moments at which the fluvographic measurements were carried out, we plotted representative curves of the variations of temperature T and thermal conductivity k_e of the peritumoral and intratumoral tissue as a functtion of the depth of implantation p of the needle probe; we then calculated the specific heat power q★ of the carcinoma.

Cutaneous thermal parameters. Using infrared as well as in some cases liquid crystals thermograms recorded before treatment and subsequently at every check examination, we graphically represented as functions of the time t: (*a*) the intensity $\Delta T1$ of the variations of the mean hyperthermia on the cancerous breast compared with the normal breast and, (*b*) the intensity $\Delta T2$ of the localised hyperthermia caused by the cancer compared with the symmetrical region. According to the thermographic symptomatology worked out by us [10], this localised hyperthermia may correspond either to a so-called hot-spot (generally intense and fairly limited) or to vascular hyperthermia (most often corresponding topographically to superficial veins).

Morphological parameters. The information provided by clinical observations and radiographic images being for the most part difficult to quantify, only the variations of the mean tumour diameter D as a function of time t were plotted. D was determined at each check examination, using the same graphical method as that previously described [9].

RESULTS AND DISCUSSION

Analysis of the changes in tumoral and cutaneous hyperthermia subsequent to radiotherapy makes it possible to distinguish from among the cases studied three types of thermal evolution, namely according as there is normalisation *(A),* regression followed by recurrence (B) or persistence of the metabolic heat production (C). We should point out that this simplified nomenclature is intended merely to facilitate the didactic presentation of the results. It is in fact completely relative as also are the clinical notions of sterilisation and non-sterilisation since the characterisation of post-radiotherapic evolution is necessarily linked to the duration of follow-up, i.e. to the distance in time from the end of the treatment.

We now propose to describe, illustrate and discuss the three types of evolution while comparing items of thermological information first with one another and then with certain clinical and radiographic data. The presentation will be concerned essentially (a) from the fundamental point of view, with the effects of ionising radiation on metabolic heat production by the cancer; (b) from the practical point of view, with the contribution of thermal methods to the decision concerning therapy and to post-irradiation follow-up. The problem of cutaneous thermal reaction to irradiation will only be dealt with summarily. The captions to the curves and pictures given by way of example will be very detailed in order to stress the semantics and the complementary nature of the various investigations.

IRRADIATION AND HEAT PRODUCTION OF THE CARCINOMA

A) Normalisation of the heat production (13 cases, example Fig. 1).

The intra- and peritumoral hyperthermia and increased blood flow as well as the cutaneous hyperthermia generally observed before treatment regress progressively after irradiation and disappear completely or almost completely. Thus the curves for the intramammary temperatures and thermal conductivities finally assume an almost normal appearance. This normalisation, however, takes place over very variable periods, namely from several months to several years depending on the particular case. The specific heat power of the cancerous tissue evolves in a manner similar to tumoral and cutaneous hyperthermia, but it decreases much more rapidly. These results confirm that ionising radiations have a reducing effect on the heat production by the cancer, i.e. therefore a braking effect on its growth [18]. Nevertheless, this effect does not take place suddenly in the course of irradiation but is progressive and spread over several weeks or even several months.

Concurrently with the thermological evolution, the original clinical and radiographic

anomalies regress more or less rapidly and completely, but regularly; the tumoral opacity, in particular, decreases like the cutaneous hyperthermia. Local sterilisation is considered to have been acquired by the end of at least five years in the absence of any sign of developmental recurrence. In seven out of thirteen cases in which thermal anomalies had disappeared completely, the tumoral opacity stabilised after having first regressed; nevertheless, sterilisation was confirmed by cytological examination and then by the long-term evolution which was favourable. Thermofluvographic investigations or, when these are impossible, thermographic investigations therefore appear capable of supplying arguments in favour of the fibrous nature of an indefinite residual opacity when heat production or cutaneous hyperthermia are characterised by continual regression.

The thirteen carcinomas considered as sterilised by radiotherapy initially showed weak heat production ($q^{\star} \leq 25.10^{-3} W/cm^3$) (Fig. 4); moreover, with the exception of two for which q* was less than $10.10^{-3} W/cm^3$, they showed metastases of the axillary lymph nodes (subsequently also irradiated). These results are in satisfactory agreement with the relation previously established between the specific heat power q*, the volume doubling time T_{2v} and the probability of lymphatic dissemination [911]. Indeed, we found that: 1) when $q^{\star} \leq 10.10^{-3}$ W/cm^3, the growth is slow ($\tau_{2V} \geq 250$ days) and there is no lymphatic invasion; 2) when $10.10^{-3} < q^{*} < 20.10^{-3} W/cm^3$, growth is still relatively slow ($\tau_{2V} \geq 150$ days), but there are usually lymph-node metastases or carcinomatous lymphangites. It should also be noted that the highest value of q* for which sterilisation was obtained ($25.10^{-3} W/cm^3$) is greater than the limit heat production beyond which growth is fairly fast and lymphatic dissemination probable. This corroborates the clinical statistics which show that radiotherapy may have beneficial effects on original cancers already presenting lymph-node metastases (provided the latter are suitably irradiated) but in which the original tumour is still not very large.

Fig. 1. **Carcinoma of the right breast, upper inner quadrant (Tl Nl MO), patient aged 59 years.**

* Radiotherapy only: ^{60}Co, tumour dose: **7800** rads, **TDF=149.**

• Post-irradiation follow-up: clinical, X-ray and thermographic check examinations approximately, 2, 3, and 14 months, then 2, 3, 4 and 5 years after end of treatment.

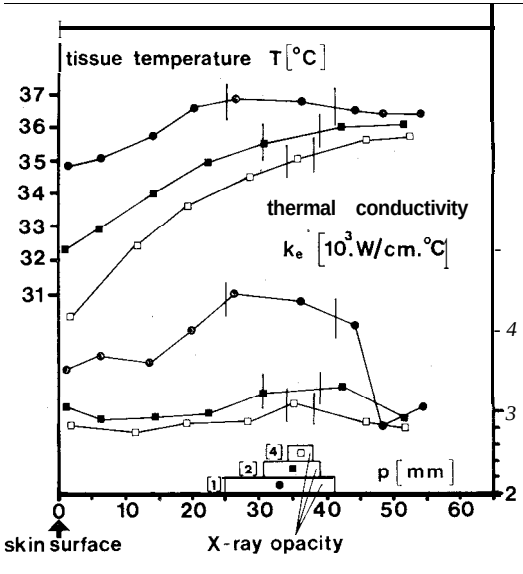


Fig. 1. A) Intratumoral thermometry and fluvography.

(Distribution oj temperature T and thermal conductivity k-function of the capillary blood flow-of the peri-and intratumorul tissues as a junction of the depth p of implantation of the thermographic needle. Hartmann and Braun Fluvograph type 2, needle probe type G1).

Before treatment (•): slight hyperthermia but markedly increased intra-and peritumoral blood flow.

6 months after end of treatment (ž): marked regression of both temperature and thermal conductivity.

4 years later (•): temperature and thermal conductivity curves of normal form without any significant increase at the site corresponding to the residual opacity.

Measurement	*Before* ^{60}Co	*6 months later*	**4 years** *a*
$\bar{D}$ (cm)	1.7	0.8	0.4
P (cm)	2.5	3.1	3.4
k_e (10^3 W/cm°C)	4.4	3.2	3.0
ΔTy (°C)	1.6	0.3	0
p* (10' W/cm³)	**16.3**	**3.7**	**0**

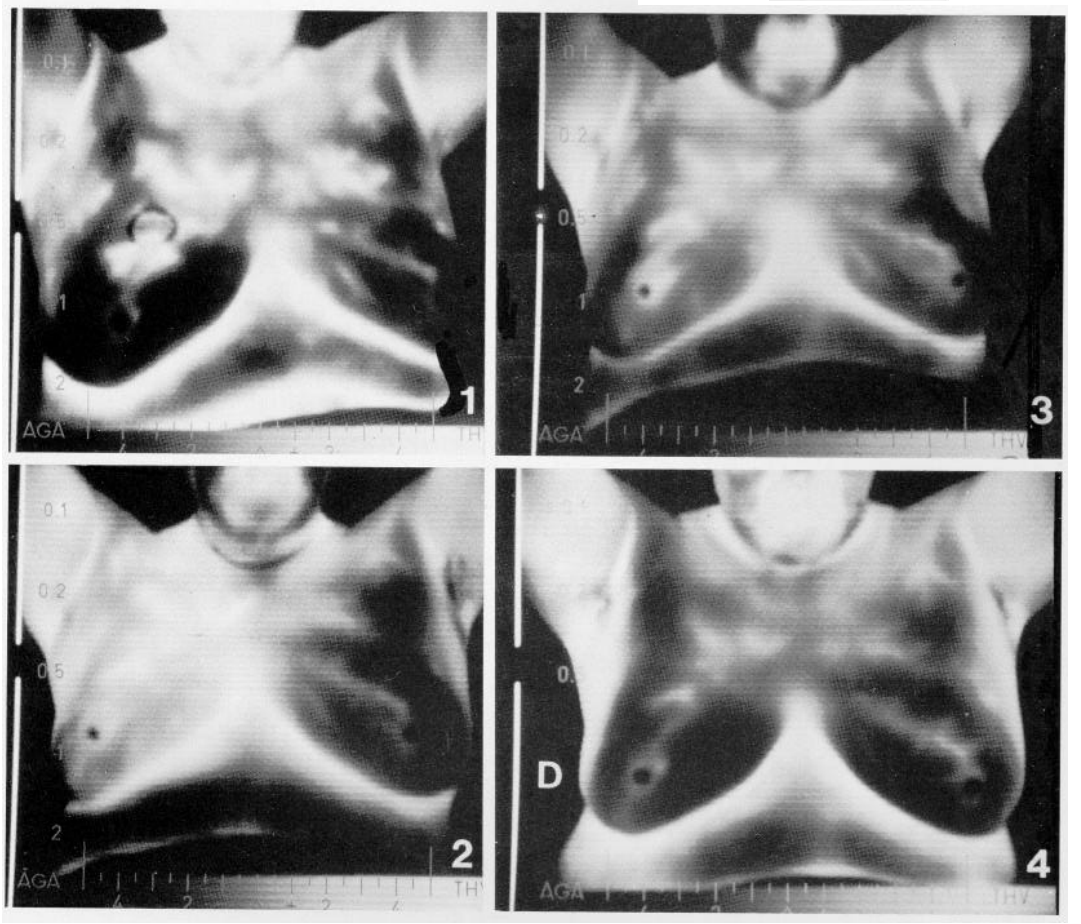


Fig. 1. B) Skin thermography (see also curves fig. 1 C).

(Images recorded with an AGA infrared Camera, type 680).

- Before treatment (1): intense hyperthermia in the upper inner quadrant of the right breast (AT2 = 4°C), corresponding topographically to the palpable lump.
- 6 months after end of treatment (2): celar decrease of the mean thermal level of the whole breast (AT1 = 2.5" C) as a result of the cutaneous effects of the irradiation.
- 14 months after treatment (3): decrease of the reactive overall hyperthermia (AT1 = 0.5" C) and continuation of regression of the malignant hyperthermia (AT2 = 1" C).
- 4 years later (4): normalisation of the thermal pattern.

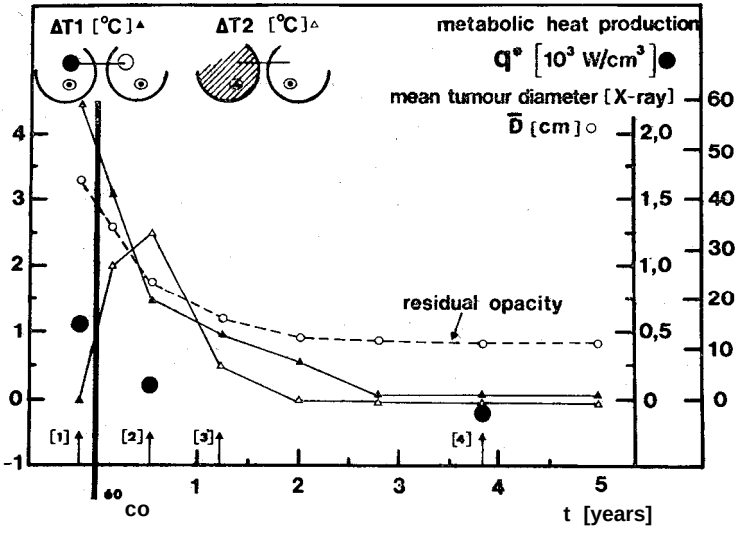


Fig. 1. **C) Skin thermometry and radiography.**

(Evolution of the intensify AT1 of the mean hyperthermia of the cancerous breast compared with the normal breast, of the intensity AT2 *of the upper inner hyperthermia compared with the symmetrical region on the controlera1 breast, and of the mean tumour diameter D. Heimann infrared bolometer, CGR Senograph).*

After the irradiation, almost concurrent regressions of AT2 and??. but faster for AT2, then stabilisation after about 3 years (cytological confirmation of the fibrous nature of the residual opacity). Temporary increase of AT1 after irradiation (see also thermogram 2 on fig. 1 B). At the 8th check examination, i.e. 5 years after the treatment, no sign of recurrence. Noteworthy is that regression of the metabolic heat production following irradiation occurs very rapidly, the decrease of q* being by about 80% 6 months after the end of treatment.

Conclusion: normalisation of metabolic heat production and blood flow as well as skin thermal pattern= sterilisation (after 5 years).

B) Regression followed by recurrence of heat production (11 cases, example Fig. 2).

The thermal and circulatory, tumoral and cutaneous anomalies regress first of all as a result of the irradiation, then they stabilise. However, at the end of a certain time ranging from several months to several years, they become progressively more marked, sometimes attaining values exceeding those measured before treatment. The specific heat power of the cancerous tissue evolves in similar way but two remarkable facts should be stressed: (a) the regression and the recurrence of metabolic heat production are always significantly faster than those of the hyperthermia; (b) the heat production, after having decreased more or less, finally attains exactly the same value as before the irradiation. On contrary to the preceding situation, the reducing effect of radiotherapy is only temporary and the heat producing potentiality of the cancer is not overcome for good. (The same phenomenon might be observed in the case of cancers in the previous category which, although considered as sterilised at the end of five years, might nevertheless recur subsequently). Morphologically, nevertheless, the tumour is halted >> by the irradiation, as is also witnessed by the curves of intratumoral thermal conductivities which frequently show zones of reduced blood flow probably corresponding to these post-irradiation ftbro-atrophic zones identified histologically by Baclesse [1].

The evolution of the tumoral opacity comprises the two same phases but the regression is a little slower and the recurrence later and much faster than those for hyperthermia and especially for metabolic heat production. Thus local recurrences were always detected at an earlier stage by thermal methods than by

Fig. 2. **Carcinoma of the left breast upper outer quadrant (T2 Nl MO), patient aged 39 years.**

- Radiotherapy only: ^{60}Co, tumour dose: 8000 rads, TDF: 155.
- Follow-up: check examinations, 2, 6, 11 and 20 months and then 2 1/2, 3, 4 and 5 years after the end of treatment.

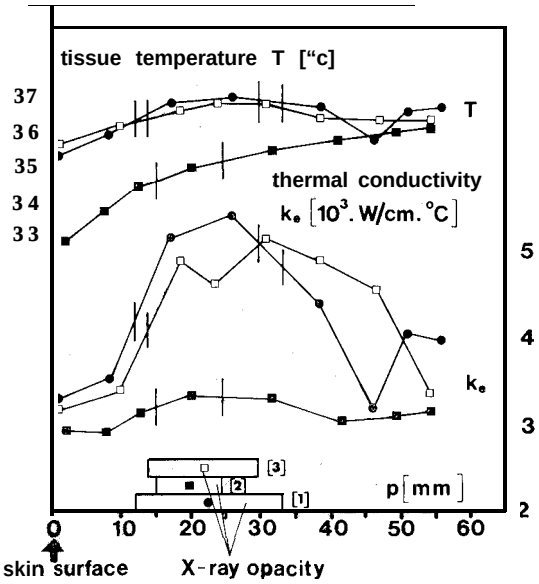


Fig. 2. A) **Intratumoral thermometry and fluvography.**

— Before treatment (a): slight tumoral hyperthermia and increased blood flow largely exceeding the limits of the tumour.

- 1 year after the end of treatment (•): apparent normalisation of temperature and thermal conductivity.

- 5 years later (•): reappearance of tumoral hyperthermia and strong increase in the blood flow especially at the periphery of the tumor. The relative decreased blood flow at the centre of the tumour probably corresponds to post-irradiation fibroatrophic zones.

Measurement	*Before ^{60}Co*	*1 year later*	*5 years later*
D (cm)	2.1	0.9	1.6
P (cm)	1.2	1.5	1.4
k_e (10^3 W/cm°C)	5.1	3.2	4.8
ΔTy (°C)	2.1	0.4	2.0
q★ (10^3 W/cm^3)	**30**	**8**	**31**

clinical examination or radiography, the time difference being variable but in most cases two years or over. We should make it clear that an opacity persisted in all these cases and that intratissular thermofluvography and cutaneous thermography only suggested the neoplastic character of the remains of the tumour. In principle, cytological examination should make it possible to confirm malignancy as soon as the recurrence has been indicated thermally, but in practice puncture with the fine needle is then often difficult because of the hardening of the tumour caused by the irradiation.

The time to local recurrence, defined as the time elapsing between the end of treatment and the recurrence of cutaneous hyperthermia, is shorter according as the specific heat power q* measured before the irradiation is higher (Fig. 4). (It was not possible to choose the time of re-increase of metabolic of heat production as reference since q* was not measured at every check examination). The eleven cancers which recurred within a period of six months to four years and a half all initially had intense heat production ($20.10^{-3} < q^* < 40.10^{-3}$ W/cm^3), i.e. probably a fairly high growth rate (corresponding values for the tumour doubling time, according to [9]: $150 > \tau_{2V} > 75$ days); furthermore, without exception they showed metastases of the axillary lymph nodes which were also irradiated *.

* From the point of view of the breast-cancer patient, or more precisely of the benefit she obtains from treatment in the form of increased life expectancy, the time to local recurrence is obviously measured in months or in years, i.e. in absolute units of astronomical time. But at the fundamental level of tumoral kinetics and effects of ionising radiation, it would be more correct to relate this period to the biological clock which is peculiar to each cancer by expressing it, for example, in periods of the cellular cycle or more conveniently as tumour doubling time. Thus in the case in which sterilisation of the cancer is not obtained: after the irradiation, the residual malignant cells start proliferating again and consequently give rise to a local recurrence which is detectable sooner according as the doubling time is shorter. The graphical representation in Fig. 4 thus in fact distorts reality with regard both to the effects of the irradiation on the cancer and to the results of radiotherapy.

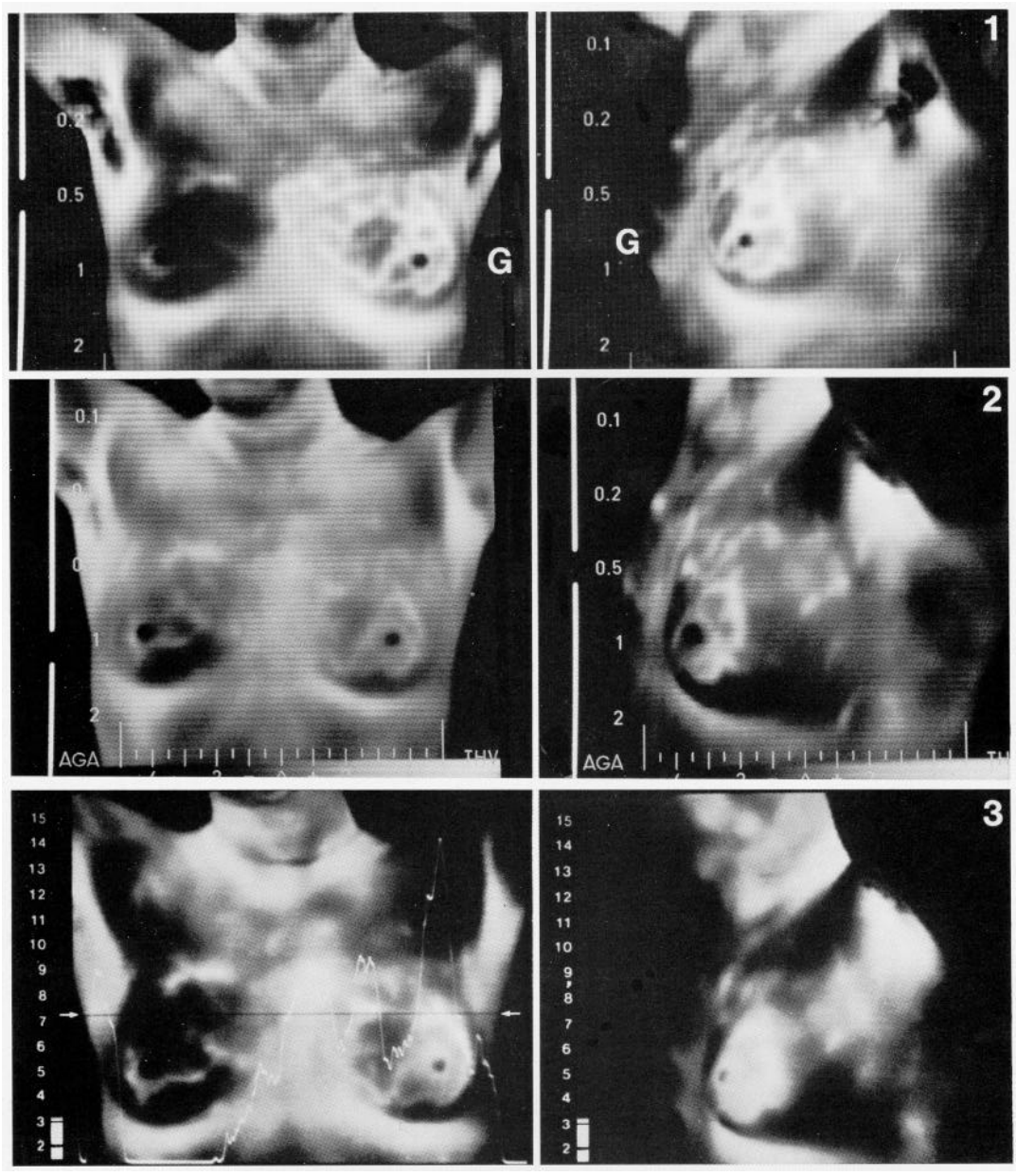


Fig. 2. B) Skin thermography.

(Thermograms recorded with an AGA infrared camera type 680-[1, 2] and a PHILIPS thermograph [3]).

— Before treatment (1): multiple vascular hyperthermia over the whole left breast, more intense in the external quadrants ($\Delta T2 = 3°$ C); overall hyperthermia of the left breast compared with the right breast ($\Delta T1 = 2°$ C).

— 1 year after treatment (2): clear decrease of the vascular hyperthermia in extent as well as intensity (AT2 = 0.5" C); the mean skin temperature is approximately the same over the two breasts.

- 5 years later (3): reappearance of intense vascular hyperthermia in the upper outer quadrant especially in the supra-areolar region (AT2 = 4.5" C, see thermal profile on the frontal thermogram); reincrease of the mean thermal level of the irradiated breast; development of a nipple hyperthermia.

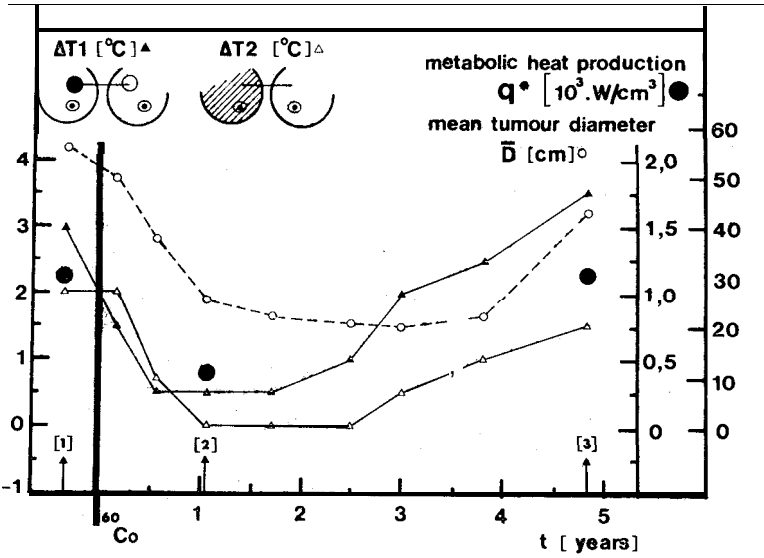


Fig. 2. C) **Skin thermometry and radiography.**

After the irradiation, concurrent regressions of the cutaneous hyperthermia ($\Delta T2$) and tumoral opacity ($\overline{D}$), then stabilisation occuring more rapidly as regards the hyperthermia; this favourable evolution was also confirmed by both local and general clinical observations. At the 5th check examination, i.e. 2½ years after treatment, the residual opacity was unchanged but the vascular hyperthermia reincreased clearly ($\Delta T2 = 1°C$). These hyperthermia were still more marked at the 6th check ($\Delta T2 = 1.5°C$) while the opacity had not varied significantly. The recurrence was only confirmed at the 8th check examination, i.e. about 5 years after irradiation, by physical and X-ray examinations. Noteworthy is that, having first decreased as a result of the irradiation, the specific heat power q★ of the cancerous tissue finally became as intense as it was before treatment.

Conclusion: Regression then re-increase of metabolic heat production and blood flow as well as skin hyperthermia = recurrence (confirmed histologically).

C) Persistance of heat production (7 cases, example Fig. 3).

In these cases the tumoral and cutaneous hyperthermia as well as the increased intra- and peritumoral blood flow regress only very little after the irradiation. Then, generally without any intermediate stabilisation phase, these anomalies intensify and spread, rapidly becoming greater than they were before treatment. The evolution of the tumoral opacity is comparable but the post-irradiation stabilisation takes longer and in particular the recurrence is always slower than that of the skin hyperthermia. Despite these thermal, circulatory and morphological changes, which though not marked are nevertheless appreciable, the metabolic heat production does not vary significantly. It should also be noted that it was very intense for the seven cancers in question ($q^* > 45.10^{-3} W/cm^3$) (Fig. 4) which all showed metastases of the axillary lymph nodes and, in two cases, also of the subclavicular lymph nodes.

The fact that the irradiation is without effect on the intrinsic thermicity of the cancer, at least on the macroscopic scale and on the scale of the times in which these phenomena are noted, differentiates this type of evolution from the preceding type. Although this result is a priori paradoxical since the temperatures, thermal conductivities and tumour sizes are affected by the irradiation, it appears plausible when we remember the significance of q* which represents the specific metabolic heat power in relation to the unit volume of the tumour [6,8]. Despite the local destruction caused by the ionising radiation, the malignant cells which survive and continue to proliferate are

Fig. 3. Carcinoma of the left breast, retro-areolar (T2 Nl MO), patient aged 55 years.

* Radiotherapy only: ^{60}Co, tumour dose: 8500 rads, **TDF=158.**
• Follow-up: 16 and 11 months, then $1^1/_2$, 2 and 3 years, after the end of treatment.

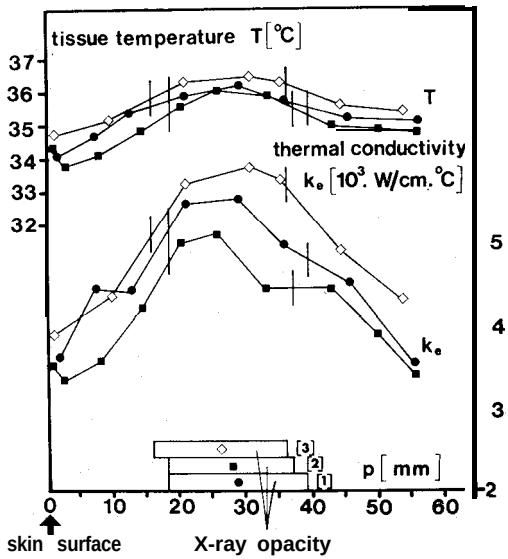


Fig. 3. A) **Intratumoral thermometry and fluvography.**

— Before treatment (●): intense intra- and peritumoral hyperthermia and strongly increased blood flow.

- 1 year after treatment (■): slight regression of temperature and thermal conductivity; slight increase in skin temperature and blood flow.

— 2 years later (◇): marked increase in the tumoral hyperthermia and blood flow, the later being more intense and more extensive than before irradiation.

Measurement	*Before "Co*	*1 year later*	*2 years later*
$\overline{D}$ (cm)	2.1	**1.9**	2.0
P (cm)	1.9	1.9	1.6
k_e (10^3 W/cm°C)	5.4	5.0	5.6
ΔTy (°C)	2.7	2.4	2.6
q★ (10^3 W/cm^3)	48.4	48.6	48.7

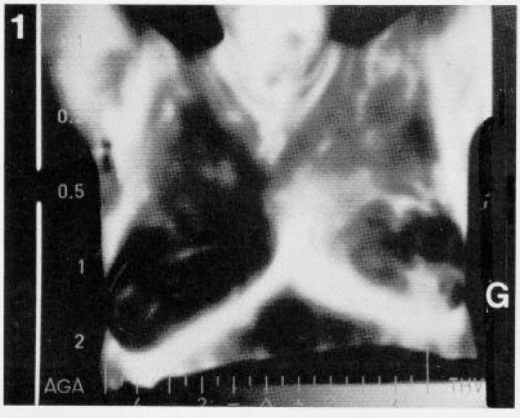
probably intact, so that their metabolism and consequently their growth and heat production are the same as if they had not been irradiated. The thermological distinction thus made between radiosensitive and radioresistant carcinomas is perfectly realistic since our patients were all irradiated under equivalent conditions. In this context, we would remind that the extreme variability of the effects of radiotherapy is an idea familiar to clinicians and to anatomopathologists but still not well understood and confusedly attributed to multiple and complex factors governing the relations between the host and the cancer [2].

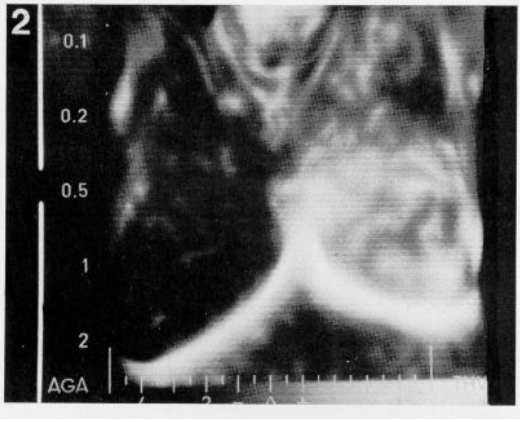
Irradiation and cutaneous thermology

Although this question is beyond the scope of the present article, we will touch upon it on account of its practical implications. Our analysis will of necessity be incomplete since the radiation doses imparted to the skin were not evaluated. The particular case of the so-called « radiotherapic breast » will not be considered, mainly due to the fact that it is difficult in these circumstances to separate the thermal effects of the irradiation on the skin, the gland and the carcinoma.

Cutaneous thermal reactions to irradiation can be divided into two groups:

Systematic hyperthermia. Even in the course of actual treatment cutaneous hyperthermia almost always occur whose topography corresponds approximately to the irradiation fields. Their intensity varies greatly from one patient to the other, despite the similarity in the conditions of treatment (Figs. 1, 2 and 3). The regression of these hyperthermia is more or less fast, but generally slower than that of the erythema. This last observation sheds some light on the way in which ionising radiations affect the skin It. It will be recalled in fact that erythema reflects an effect on the capillary bed (opening of the precapillary sphincters), while the hyperthermia indicates an effect on the dermal vascular plexuses (arteriolar vasodilatation) [5].





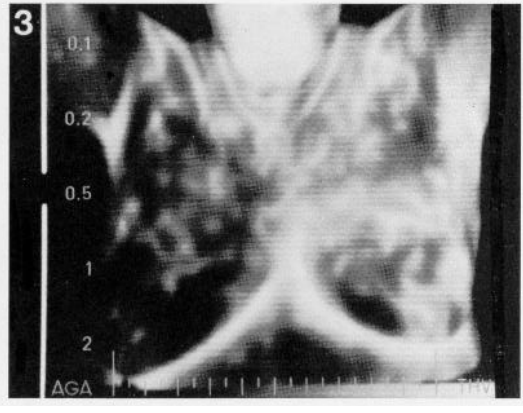


Fig. 3. **B) Skin thermography.**

— Before treatment **(1):** intense hyperthermia in the internal areolar region (AT2 = 4" C), hyperthermia of the nipple, overall hyperthermia of the cancerous breast compared with the controlateral breast (AT1 = 1.5" C).

- 1 year later (2): slight regression of the areolar hyperthermia (- 0.5 °C) and accentuation of the vascular hyperthermia over the whole breast; marked increase in the mean temperature corresponding to the cutaneous effects of irradiation (AT1 = 3" C).
- 2 years later (3): persistance of the areolar hyperthermia; clear changes in the thermovascular pattern, the vascular hyperthermia being markedly increased in the supra-medial and upper outer areas.

Accidental hypertermia. These hyperthermia are noted only in certain cases and are pathological when they are due to glandular or cutaneous consequences of irradiation (sclero-oedematous sequela, telangiectasies), or morphological when they correspond to depressions created by tissular retractions (concave skin areas are generally hyperthermal compared with the adjacent areas as a result of a reduction of the heat loss radiation and convection between the skin and the surroundings). Usually, these hyperthermia are very intense and persist for a long time or even indefinitely. Sometimes they are in the same region of the breast as the malignant hyperthermia observed before the irradiation. In most cases, their etiology is easy to determine at hand of confrontations between the thermograms and the clinical and radiological findings.

HEAT PRODUCTION, DECISION REGARDING THERAPY, POST-IRRADIATION SURVEILLANCE AND RESULTS

In previous studies [9, 14] we have shown the prognostic value of the metabolic heat production and the associated hyperthermia of the skin and thereby justified the part which thermal methods now essentially play in the establishment of the pre-therapeutic prognosis of breast carcinomas. As an extension to those conclusions, the foregoing results assume a great importance at practical level from the following two points of view:

The decision regarding therapy. Irradiation conditions being equal, radiotherapy locally sterilises carcinomas with a low heat production while it has no beneficial effect on carcinomas with intense heat production. These

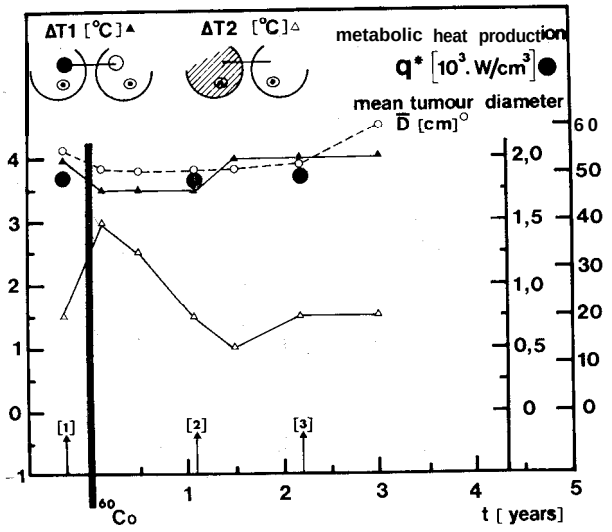


Fig. 3. **C) Skin thermometry and radiography.**

At the 1st check examination, i.e. 1 month after the end of treatment, the skin hyperthermia and the tumoral opacity had scarcely regressed. Subsequently, after stabilisation lasting over 1½ year, the thermal and X-ray anomalies became more marked finally becoming greater than before the irradiation. The re-increase of the skin hyperthermia preceded clearly that of the X-ray opacity by about a year. It should be noted that the irradiation had no noticeable effect on the metabolic heat production, q* having approximately the same value before and after radiotherapy.

Conclusion: persistence of high tumoral heat production and blood flow, and increase of skin hyperthermia = non-sterilisation.

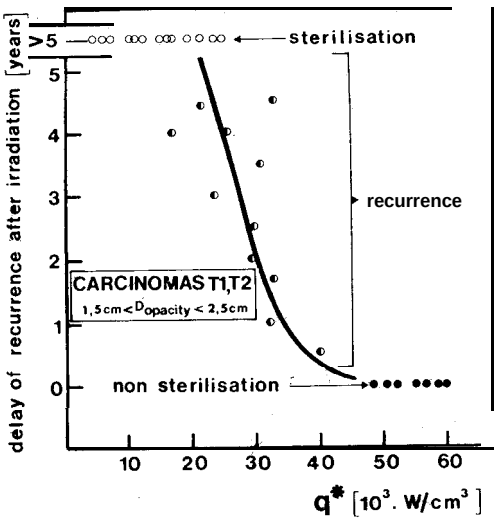


Fig. **4. Relation between the specific metabolic heat production of breast carcinomas (q*) and the time to recurrence after irradiation, as determined for a homogeneous group of 31 cancers (T1, T2), treated exclusively by radiotherapy (60Co) under equivalent conditions.**

The zero periods (●) correspond to cases in which the irradiation had no appreciable effect on the tumour. The times stated (0) correspond to local recurrences detected first by skin termography. Where no times are shown (◐), there was no sign of recurrence at the check made at least five years after the end of treatment.

clinical facts were to some extent foreseeable since tumour growth is faster and the probability of lymphatic dissemination greater - i.e. the prognosis all the more unfavourable - according as the metabolic heat production is higher. The thermal characteristics of the tumour consequently constitute an objective criterion for the decision regarding therapy, at least in the case of small carcinomas: (a) when the tumour heat production and the skin hyperthermia are low, either tumorectomy or radiation can be chosen, provided their respective advantages are considered and also the criteria peculiar to each individual case; *(b)* when the tumour heat production and the skin hyperthermia are intense, radiotherapy should be recommended and the local excision of the growth (tumorectomy) prohibited, considering the high probability of rapid growth rate and lymphatic invasion.

Post-irradiation surveillance. Whatever the type of evolution, the following two complementary observations are relevant: (a) the long-term agreement between the thermal evolution of the irradiated carcinoma and the loco-regional results of the treatment; *(b)* the earliness of the regression or of the re-increase of heat production and skin hyperthermia in relation to the corresponding clinical and ra-

diographic variations. This applies, in fact, not just to the limited sample formed by the cases studied here but to all irradiated carcinomas in general, as we showed upon the basis of a statistical study involving 1138 carcinomas irradiated in our Hospital Department in the course of 1968, 1969, 1970 and 1971 [13, 14]. In situ thermofluvography and skin thermography are thus shown to be suitable for forecasting the longterm results, favourable or unfavourable, of irradiation. In particular, the very early thermological indication of non-sterilisation or recurrence is vitally important because it enables a decision regarding repair surgery to be taken at an earlier moment.

Two important observations of a methodological nature are relevant here, concerning:

The appreciation of the results of irradiation. All statistics intended to depict the effectiveness or otherwise of radiotherapy of carcinomas are concerned essentially with the percentages of sterilisation within definite periods of five or ten years, expressed in terms of the TNM clinical classification.

This is a useful measure when it is the only one possible but it is really not very significant and distorts the results, for the following reasons: (a) the TNM classification is representative of the stage reached by the carcinoma at the moment of the diagnosis but tells us nothing about its potential for development (with the possible exception of certain T4 forms); *(b)* the five- and ten-year periods are absolute and make no allowance for the extreme variability of growth rate from one carcinoma to another. Let us take the case of two irradiated carcinomas, initially classified in the same clinical category Tl Nl MO, but with different doubling times: conventional statistics cannot draw any distinction between these two cancers, although the probability of early local recurrence is much greater for the carcinoma with the fast growth rate than for the one with the slow growth rate. Since the doubling time is not measurable under normal clinical conditions, it would be wise henceforth also to express the results in terms of metabolic heat production or skin hyperthermia, whose intensity is inversely proportional to the doubling time [9].

The use of skin thermography for surveillance. From the point of view of post-irradiation follow-up, the skin hyperthermia visualised by infrared scanners or liquid-crystal devices are less significant than the specific heat power of the cancer determined in situ by thermofluvographic measurements. In fact, these hyperthermia merely reflect, with a slight delay, namely of the order of several weeks to several months, the thermal signs of the effects of irradiation on the tumour; furthermore, their intensity is not an unambiguous function of the specific heat power [9]. However, since only a limited category of carcinomas can be investigated intratumorally and these investigations take a fairly long time, only skin thermography, despite some inadequacies, can be used as a systematic follow-up method [13, 14, 16]. We have already discussed this problem in detail when it arose in a similar fashion at the stage of the thermological assessment of the pre-therapeutic prognosis [9]. Because of the thermal reactions of the skin to irradiation (see preceding paragraph), the interpretation of the thermograms of the irradiated breast presents a number of difficulties. Erythematous hyperthermia is not very troublesome since the phenomenon is practically constant and regresses rapidly, generally in a matter of months. Accidental hyperthermia, on the other hand, are snares and have to be distinguished very carefully from malignant hyperthermia by comparing them meticolously with the clinical and radiographic findings.

REFERENCES

1. BACLESSE F., GRICOUROFF G., TAILHEFER A.: Essai de röntgentherapie du cancer du sein suivi d'opération large. Résultats histologiques. *Bull. Assoc. Franç. Cancer*, **28**, 729, 1939.
2. BARBIN J., BONNARD J., GUIHARD R., MARRIONNEAU J.: Action histologique du radio-cobalt dans les épithéliomas du sein sur la tumeur primaire et les ganglions axillaires. Relation avec la survie à cinq ans. In: Therapeutiques non mutilantes des cancércuscs du sein, Ch. GROS, ed. Masson, *Paris*, p. 137, 1974.
3. CALLE R., PIERQUIN B.: La radiothérapie locorégionale seule: Principes d'irradiation in: Thérapeutiques non mutilantes des cancéreuses du sein, ed. by Ch. GROS, Masson, Paris, p. 83, 1974.
4. ELLIS R.: Fractionation in radiotherapy. In: modern trends in radiotherapy, vol. 1. Deeley et Wood, ed., Butterworth, London, p. 34, 1967.
5. GAUTHERIE M.: Etude de la régulation thermique cutanée locale chez l'homme par la

méthode de la thermoconvectance. Mise en évidence d'un mécanisme coopératif histaminobradykininique. *J. Physiol.*, **63**, 41, 1971.
6. GAUTHERIE M., BOURJAT P., QUENNEVILLE Y., GROS Ch.: Puissance thermogène des épithéliomas mammaires. I. Détermination par thermométrie intratumorale et thermographie infrarouge cutanée. *Rev. Europ. Etud. Clin. Biol.*, **17**, 776, 1972.
7. GAUTHERIE M., GROS Ch., BOURJAT P., QUENNEVILLE Y.: Puissance thermogène des carcinomes mammaires. II Variations lors d'épreuves hormonales. *Biomédecine*, **18**, 421, 1973.
8. GAUTHERIE M., QUENNEVILLE Y., GROS Ch.: Thermogénèse des carcinomes mammaires. III. Etude par fluvographie de la conductibilité thermique des tissus mammaires et de l'influence de la vascularisation tumorale. *Biomédecine*, **23**, 237, 1975.
9. GAUTHERIE M., ARMAND M. O., GROS Ch.: Thermogénèse des carcinomes mammaires. IV. Etude lors d'évolutions spontanées de l'influence de la vitesse de croissance et des corrélations avec la dissémination lymphatique. *Biomedicine*, **22**, 323, 1975.
10. GAUTHERIE M., HAEHNEL P., GROS Ch.: Thermogénèse des carcinomes mammaires. V. Etude des effects de la radiothérapie ^{60}Co et des corrélations avec l'espérance de stérilisation. *Biomédecine*, **22**, 416-427, 1975.
11. GAUTHERIE M., QUENNEVILLE Y., GROS Ch.: Metabolic heat production, growth rate and prognosis of early breast carcinomas. In: Functional Explorations in Senology, ed. by C. COLIN et al. (Proceed. Internal. Symp. Liège-Belgium, nov. 1975), European Press, Ghent-Belgium, 93-110, 1976.
12. GROS Ch., GAUTHERIE M., ARCHER F.: Séméiologie thermographique des épithéliomas mammaires. *Bull. Cancer*, **58**, 69, 1971.
13. GROS Ch., GAUTHERIE M., BOURJAT P., WARTER F., WAILLE Y.: Thermographie des cancers du sein irradiés. *Bull. Cancer*, **58**, 445, *1971.*
14. GROS Ch., GAUTHERIE M., BOURJAT P.: Pretherapeutic prognosis and post-therapeutic follow-up of breast cancers by thermography. In: Proceedings 1" Europ. Congr. Thermography N. J. M. Aarts, M. Gautherie, E. F. J. Ring ed., Karger, Basel, 77, 1975.
15. LACASSAGNE A., GRICOUROFF G.: in: Action des radiations ionisantes sur l'organisme, Masson, Paris, 21, 1956.
16. LEVRAUD J., ROBERT F., AMALRIC R., SPITALIER J. M.: Surveillance thermovisuelle des cancers du sein traités par irradiations exclusives. *Corse Med.*, **2**, 68, 1973.
17. ORTON C. G., ELLIS F.: A simplification in the use of the NSD concept in pratical radiotherapy. *Brit. J. Radiol.*, **46**, 529, 1973.
18. TUBIANA M., DUTREIX J., DUTREIX A., JOCKEY P.: in: Bases physiques de la radiothérapie et de la radiobiologie. Masson, Paris, 599, 1963.