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Physical parameters in thermal imaging of basal cell cancer patients treated with high-dose-rate brachytherapy — first study

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ABSTRACT

Background: The basal cell carcinoma (BCC) is often treated by surgery or radiotherapy using ionizing radiation. While there is an established diagnostic path before treatment and also for the follow-up there are no good noninvasive methods objectifying irradiated area evolution during treatment. The main goal of preliminary studies was to try to answer if there are any useful information that can be derived from temperature effects of high-dose-rate (HDR) brachytherapy in treatment of BCC. Moreover, the temperature gradient was introduced as a physical parameter characterizing the thermal map of the lesion, its surroundings and reference area, which provided information about cancer tissue thermal reaction to brachytherapy.

Materials and methods: Thirty-three patients suffering from BCC were monitored with thermovision during the brachytherapy treatment. All lesions were diagnosed as superficial and were confirmed with histopathology examination.

Results: Results of the study showed two groups of patients characterized with two thermal maps and temperature gradient describing the lesion and surrounding area of BCC. The first group was characterized by higher temperature of the lesion than the surrounding tissue temperature (mean dT = 0,41°) whereas the other one, with lower lesion temperature (mean dT = –0.42°). It seems that the temperature changes observed in designated areas before and after therapy may provide physicians with additional information which could be useful in planning the treatment process, especially when considering temperature gradient changes during therapy.

Conclusions: Although the data obtained indicate the possibilities of temperature distribution in pre-irradiation cases, further research is required for estimation of clinical effects of treatment.

Key words: thermal imaging; basal cell carcinoma; thermovision diagnostics

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Introduction

Non-melanoma skin cancers are the most common malignant neoplasms in Caucasians [1, 2]. This type of lesions rarely leads to metastases and patient death [3–7]. The exception are people undergoing chronic immunosuppression or with genetic predisposition to develop skin cancer induced by ultraviolet radiation. Probability of aesthetic defects, such as infiltration and destruction of adjacent tissues, is also a significant clinical problem. Such occurrences can significantly reduce the quality and comfort of patient's life. Basal cell carcinoma (BCC) is the most common skin cancer, accounting for approximately 80% of all non-melanoma skin cancers [3, 4, 8]. It arises from the cells of the basal layer of the epidermis and is characterized by slow growth and local malignancy. Most often, BCCs are located in the head and neck area [7–10]. In 90% of cases, cancer occurs between the hairline and the upper lip [11]. It can also affect the arms, back, and back of the hands. It shows an increasing tendency with the age of patients, and most disease cases are observed in the eighth decade of life, but they are also reported in younger patients, even adolescents [5].

There are various guidelines available that describe diagnostic evaluation, treatment possibilities and follow-up [12, 13]. Surgery, particularly Mohs surgery, remains the standard of care for skin cancer patients; however, interest in radiation therapy increases. One of the irradiation techniques used in the treatment of basal cell carcinoma is high-dose-rate brachytherapy (HDR BT). It is effective in either primary, adjuvant or recurrence treatment. It is an alternative for patients who cannot undergo surgery due to comorbidities, age or lack of consent [12, 14]. Brachytherapy provides a radiation dose precisely due to the positioning of the radioactive isotope inside (interstitial brachytherapy) or near the tumour (surface brachytherapy) [14, 15]. High conformity of this method allows better protection of healthy tissues surrounding the tumor. However, acute and late complications are observed, including itching, redness, peeling, ulceration, bleeding, telangiectasia or fistula.

Tumour growth is affected by cells' division and microenvironmental changes, mainly growing vasculature; hence local metabolism rises [16]. Such processes increase the temperature in soft tissue and may reflect on the skin surface as a specific thermal map. That is why thermovision may be helpful in imaging skin lesions as a quick and non-invasive tool for examination. As many publications show, thermal imaging may indicate potentially cancerous areas characterized by different average temperatures compared to healthy skin temperatures. Thermal imaging seems to be a good technique to evaluate the energy administered to the tissue due to radiation therapy due to increased energy production in the affected and then irradiated area and, consequently, increased body temperature [10, 17–22]. However, at present, thermovision cannot be used as the sole diagnostic method. Therefore, research is needed to confirm the usefulness of using thermal imaging.

Materials and methods

The Bioethics Committee approved the study at the Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw. All patients gave their informed written consent. The study was carried out by the Faculty of Science and Technology, University of Silesia, Chorzów, in cooperation with the Department of Brachytherapy, Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice Branch.

Patients

The analyzed group included 33 patients (17 female and 16 male) with histopathologically confirmed BCC in the head area. Every patient was treated using a custom-made mould applicator based on the individual anatomic features. A three-dimensional HDR-BT CT-based treatment plan was prepared. A total dose of 45 Gy in 9 fractions was prescribed 5 mm from the applicator surface; however, dose optimization was used depending on anatomy or organs at risk, e.g., eyeball, bones, a curvature of the area. Fractions were delivered twice a week. During the treatment and one month afterwards, each patient was requested to avoid physical exercise, stimulants, smoking, alcohol or hot drinks for at least 3 hours before thermal imaging diagnosis [22].

Methodology

Before thermovision, the examined patient should rest a minimum of 15 minutes under con-

trolled conditions. Any physical activity may increase blood flow and metabolism's processes affecting the thermovision. The examined areas should not be covered with clothes or bandage while waiting for the exam to get accustomed to the surrounding temperature [23].

The thermal imaging examination was carried out twice: up to two weeks before treatment start and a month after the delivery of the last treatment fraction.

It should be noted that the researchers tried to avoid of different undesirable skin reactions. That is why directly or several days after treatment, due to exudate, radiation reaction, ulceration, or other effects of BT, it was difficult to clearly define the area that should be subjected to thermal imaging measurements. Therefore, we focused on the temperature effects occurring in the treated tissues before and one month after the brachytherapy.

Every time thermal and digital photos of the treated area with its surrounding healthy tissue and the reference area were taken. Reference area was defined as the symmetric area to the neoplastic lesion, with the axis of symmetry defined as the sagittal axis of human body. A similar methodology was used by Flores Sahagun et al. [24]. According to the protocol, the irradiated area was marked as the T area, the area approximately 2cm around (depending on the place of lesion) the T area as the S area. The reference area was marked as the R area.

Each thermal image was correlated with a digital photo of the examined area. The T and the R areas were identified in the thermal image and outlined with the help of a physician.

The tests were carried out using a Flir Systems E60 thermal imaging camera with the following parameters: sensitivity < 0.05°C, refreshing sensitivity 60 Hz, detector resolution 320 × 240 pixels. Measurements were made in a room with a stable temperature (23.0 ± 1°C) and a humidity of 50%. Moreover, thermal camera was set perpendicular to the body surface and the distance between the camera and body was fixed at 0.5 meter according to the standards of thermal imaging diagnostics in medicine [22, 24].

Data analysis

ThermaCAMResearcher Professional 2.10 program was used to analyze the thermograms. The obtained thermal images were presented using the Medical scale.

Statistical analysis was performed in Microsoft Office Excel 2013 and Statistica.

During data analysis corresponding differences has been calculated:

$$dT_{TS} = T_{Target} - T_{Surroundings} \quad (1)$$

$$dT_{TR} = T_{Target} - T_{Refference} \quad (2)$$

$$dT_{SR} = T_{Surroundings} - T_{Refference} \quad (3)$$

Results

Figure 1 presents the patient's thermal images with delineated analysed areas, T, S and R. Figure 1A was obtained before, while Figure 1B was taken one month after brachytherapy treatment.

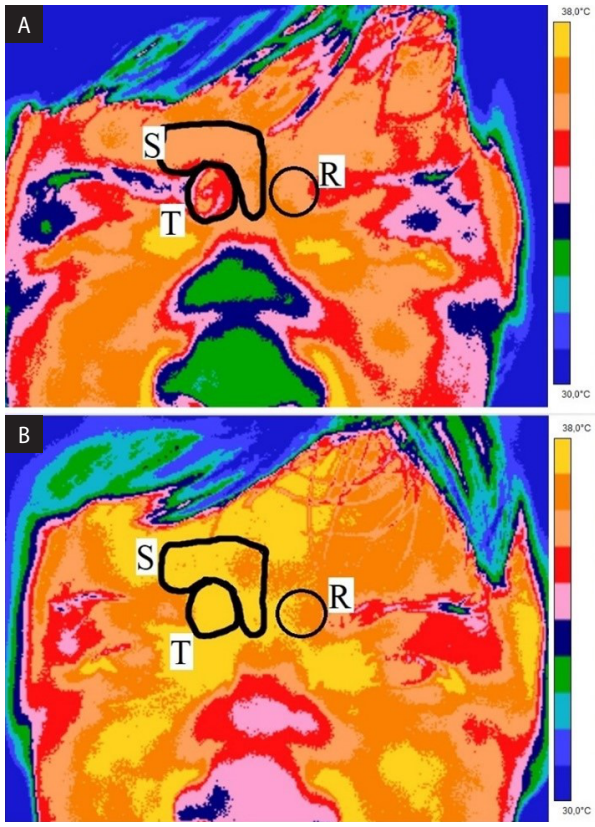

Figure 1. Thermal imaging of one of analysed patient delineated areas. T area of the neoplastic lesion (T) and surrounding area — S performed before (**A**) and 1 month (**B**) after treatment. Also marked reference (R) areas performed before (**A**) as well as 1 month after treatment (**B**)

Table 1. Temperature values derived from regions of interest for all studied group of patients

Temperature before treatment [°C]			Temperature after treatment [°C]			Difference in temperatures before treatment [°C]			Difference in temperatures after treatment [°C]		
Target	Surrounding	Reference	Target	Surrounding	Reference	Target-Surrounding	Target-Reference	Surrounding — Reference	Target-Surrounding	Target-Reference	Surrounding — Reference
35,3	35	36,2	36,7	36,6	35,7	0,3	–0,9	–1,2	0,1	1	0.9
34	33,6	30,4	36,6	36,3	34,2	0,4	3,6	3,2	0,3	2,4	2.1
37,3	36,4	36,9	36,9	36,5	37	0,9	0,4	–0,5	0,4	–0,1	–0.5
34,5	34,3	35	36,8	36,4	36,8	0,2	–0,5	–0,7	0,4	0	–0.4
36,4	36,5	36,5	35,1	35,6	35,9	–0,1	–0,1	0	–0,5	–0,8	–0.3
34,2	33,7	34,8	32,1	31,7	33,2	0,5	–0,6	–1,1	0,4	–1,1	–1.5
34,1	34,2	34,3	36,7	36,5	36,3	–0,1	–0,2	–0,1	0,2	0,4	0.2
35,7	36	35,3	34,8	34,9	34,4	–0,3	0,4	0,7	–0,1	0,4	0.5
36,1	35,9	36,6	37	36,9	36	0,2	–0,5	–0,7	0,1	1	0.9
36,2	35,5	34,3	nd	nd	nd	0,7	1,9	1,2	0,2	0,2	0
34,9	35,4	35,3	35	35,3	34,9	–0,5	–0,4	0,1	–0,3	0,1	0.4
35,2	35	34,6	33,9	33,5	33,7	0,2	0,6	0,4	0,4	0,2	–0.2
35,7	35,1	35,5	36,6	36,4	35,2	0,6	0,2	–0,4	0,2	1,4	1.2
36,4	36,3	35,5	36,5	36,4	35,8	0,1	0,9	0,8	0,1	0,7	0.6
34,9	34,5	34,5	35,1	34,9	35	0,4	0,4	0	0,2	0,1	–0.1
35,6	35,4	34,3	36	36,1	34,7	0,2	1,3	1,1	–0,1	1,3	1.4
34,8	34,9	36	34,5	33,8	36	–0,1	–1,2	–1,1	0,7	–1,5	–2.2
34,7	32,9	33,9	32,9	30,9	34,5	1,8	0,8	–1	2	–1,6	–3.6
35,3	35	34,9	36,8	35,3	35,8	0,3	0,4	0,1	1,5	1	–0.5
34,2	34,3	34,2	36,4	35,7	36	–0,1	0	0,1	0,7	0,4	–0.3
33,4	34,9	32,9	36,8	35,9	36,3	–1,5	0,5	2	0,9	0,5	–0.4
35,9	36	35,8	32,4	32,3	35	–0,1	0,1	0,2	0,1	–2,6	–2.7
33,6	32,4	31,9	34,5	35,7	33,3	1,2	1,7	0,5	–1,2	1,2	2.4
35,5	35,1	35,1	37,2	36,8	36,6	0,4	0,4	0	0,4	0,6	0.2
33,8	34,1	34,3	31,7	30	33,1	–0,3	–0,5	–0,2	1,7	–1,4	–3.1
35	35,5	35,5	37,9	37,7	37,5	–0,5	–0,5	0	0,2	0,4	0.2
36,7	36,5	36,5	36	35,5	35,1	0,2	0,2	0	0,5	0,9	0.4
35,3	36	36,1	37,4	37,3	37,4	–0,7	–0,8	–0,1	0,1	0	–0.1
35,4	35,3	35,7	36	35,9	36,7	0,1	–0,3	–0,4	0,1	–0,7	–0.8
35,3	34,7	34	36	35,7	34,7	0,6	1,3	0,7	0,3	1,3	1
36,2	36,5	36,5	36	36,3	35,1	–0,3	–0,3	0	–0,3	0,9	1.2
34,5	35,5	35,8	36,8	37,4	35,7	–1	–1,3	–0,3	–0,6	1,1	1.7
35,1	35,3	35	35,9	36,2	35,8	–0,2	0,1	0,3	–0,3	0,1	0.4

All collected data is presented in Table 1. Initial analysis (data from Tables 1 and 2) yielded no statistically significant results.

In the next step, we classified patients into two subgroups according to obtained temperature gradient between lesion and its surroundings (dT_{TS}).

The first group included 23 patients with positive dT_{TS} recorded before HDR-BT (the temperature of the lesion was higher than its surroundings). One month after HDR-BT, the temperature of the lesion significantly decreased ($p = 0.038$) (Fig. 2). The other group of 14 patients had negative dT. In those patients, T area temperature

Table 2. Analysis of obtained results from study group

	Before treatment			After treatment		
	Target	Surrounding	Reference	Target	Surrounding	Reference
Average temperature	35.19	35.08	34.97	35.66	35.39	35.42
SD	0.93	1.01	1.37	1.60	1.86	1.17
SE	0.15	0.16	0.22	0.26	0.30	0.19
Temperature differences	Target — Surrounding	Target — Reference	Surrounding — Reference	Target — Surrounding	Target — Reference	Surrounding — Reference
Average Temperature	0.11	0.22	0.10	0.27	0.24	–0.03
SD	0.61	0.98	0.84	0.62	1.03	1.29
SE	0.10	0.16	0.14	0.10	0.17	0.22

SD — standard deviation; SE — standard error

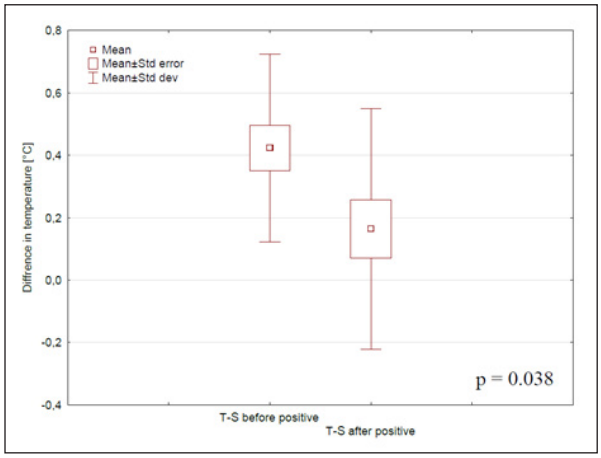

Figure 2. The temperature changes calculated as $dT_{TS} = T_{Target} - T_{surroundings}$ obtained in the group of patients with positive dT performed before and after brachytherapy (BT)

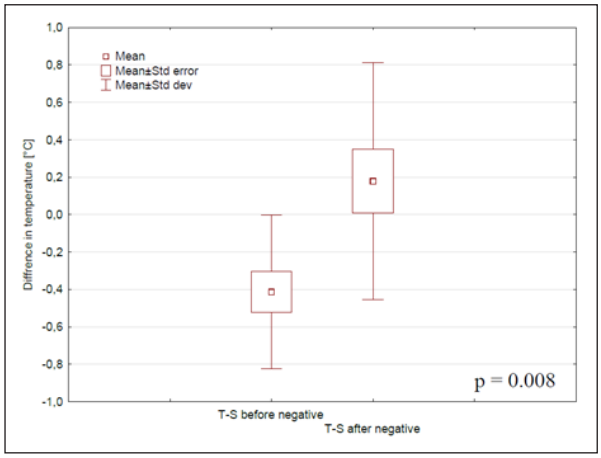

Figure 3. The temperature changes calculated as $dT_{TS} = T_{Target} - T_{surroundings}$ obtained in the group of patients with dT negative before and after brachytherapy (BT)

raised significantly after HDR-BT (p = 0.008) (Fig. 3).

Discussion

The main goal of performed pre-studies was to try answer if there are any useful information that can be derived from temperature effects of HDR brachytherapy in the treatment of basal cell carcinoma. Moreover, a physical parameter taking into account the temperature of the lesion, its surrounding as well as reference area was introduced.

All studied patients suffering from BCC were examined using Infrared Thermography during the brachytherapy. The neoplastic lesion itself was drawn each time before and after BT.

Treatment effects monitoring is essential in cancer care as well as calculating possible side-effects (NTCP0). Patients with BCC who are non-surgical candidates may profit from a method that brings valuable data on the treatment efficacy at an early stage. Thermovision has features that may provide these. It is non-invasive, easy and reliable. The main issue is which data have an impact on different clinical decisions. Our initial analysis performed on the whole studied group (all studied patients as one group) did not find any significance in the temperature changes in the treated area. The significant changes in temperature parameters were only obtained when the specific and characteristic (as was shown) temperature gradient behavior between the tumour and surrounding tissues was consid-

ered. It should be noted that there are patients with positive dT_{TS} with an average temperature difference of 0.3°C and those with negative dT_{TS} of 0.6°C. In the case of the first group, HDR-BT leads to the decrease of the temperature gradient. On the other hand, the temperature behavior in the other group rises. It should be noted that observed temperature differences in both groups result in the alignment of studied areas temperature, which may suggest a healing process.

Trying to explain the origins of such different temperature responses, we should consider the effects of ionizing radiation and the clinical and morphological characteristics of the tumour itself. Ionizing radiation damages cells, causing radiolysis of water and the avalanche production of extremely reactive free radicals. Although direct death of a cell is possible through necrosis, apoptosis or autophagy, irradiation does not usually destroy the cell immediately. A damaged cell may appear morphologically unchanged. It may continue to function for some time or even perform cell division (i.e., mitotic death). Thus, the process of tumour disappearance after the application of HDR-BT may take place at a different time rate. There are different paths of cancer cell death and different biochemical mechanisms which vary among individuals.

Moreover, inflammatory reactions may occur in the case of tissue necrosis [25–27]. This reaction may lead to a specific temperature map of the body surface. Clinically, BCC has four main variants: superficial spreading, nodular, sclerosing and pigmented. BCC lesions may contain dilated vessels (telangiectasia) or melanin. Advanced tumors may ulcerate. Different structures and specificity of growth may also contribute to the occurrence of positive and negative temperature gradients in the analyzed group.

Even though our data are unique and pioneering, there is no clear answer to what dT may provide in everyday clinical practice, which requires further investigation. This method should be added to dermoscopy and included in the HDR-BT prospective trial to correlate its features with different variants of BCC and local control.

Conclusions

Thermal imaging may provide new quantitative information about thermal reactions of skin to ionizing radiation that were differentiated by temperature gradient between the lesion and its surrounding which may yield positive and negative values. The possibilities of temperature distribution in pre-irradiation cases might become one of parameters for estimation of clinical effects of standard treatment although this subject requires further research.

The results obtained from the study should be prospectively correlated with local control and dermoscopy and confirmed on bigger group of patients.

Institutional Review Board Statement

Approval of the Polish Bioethics Committee number 38/2016.

Conflict of interests

None declared.

Funding

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