Review Article

Mechanisms of Laser-Tissue Interaction: II. Tissue Thermal Properties

Mohammad Ali Ansari, Mohsen Erfanzadeh, Ezeddin Mohajerani

Laser and Plasma Research Institute, Shahid Beheshti University, Tehran, Iran

Abstract:

Laser-tissue interaction is of great interest due to its significant application in biomedical optics in both diagnostic and treatment purposes. Major aspects of the laser-tissue interaction which has to be considered in biomedical studies are the thermal properties of the tissue and the thermal changes caused by the interaction of light and tissue. In this review paper the effects of light on the tissue at different temperatures are discussed. Then, due to the noticeable importance of studying the heat transfer quantitatively, the equations governing this phenomenon are presented. Finally a method of medical diagnosis called thermography and some of its applications are explained.

Keyword: Lasers; Tissues; Absorptions

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***Corresponding Author:** Mohammad Ali Ansari, PhD; Laser and Plasma Research Institute, Shahid Beheshti University, Tehran, Iran; Tel: +98-2129904014; Fax: +98-2122431775; Email: m_ansari@sbu.ac.ir

Introduction

As it was emphasized in the previous review article[1], lasers are widely used in biology and medicine and the majority of the hospitals utilize modern laser systems for diagnostic and therapeutic applications. The medical laser applications are defined by the type of interaction between laser light and tissues. Knowledge of laser-tissue interaction can help doctors or surgeons to select the optimal laser systems and to modify the type of their therapy[1-3]. Therefore, we seek to review the mechanisms of laser- tissue interaction. In reference number 1, the optical properties of biological tissue such as absorption, scattering, penetration and fluorescence have been reviewed[1]. In this paper, we intend to study the thermal properties of the biological tissues. During all medical applications based on heating such as hair removal, cancer therapy or laser-induced interstitial thermotherapy (LITT), it is desirable to have a complete knowledge of temperature distribution in the tissue. Study of this temperature distribution requires knowledge about the thermal properties of biological tissues. The transportation of thermal energy in biological tissues is a complicated procedure including different phenomenological mechanisms such as thermal conduction, convection, radiation, metabolic activities and phase change[2]. If a biological tissue is illuminated by a laser light such as Neodymium-Doped Yttrium Aluminium Garnet (Nd:YAG) or Carbon Dioxide (CO_2) laser, one can see multiple effects like coagulation, vaporization, carbonization or melting. These effects depend on the peak power and wavelength of the laser as well as the thermal properties of biological tissues. In Figures 1-5, these thermal effects are shown.

In 1967 Dr. Kelly published the first paper about laser coagulation. He applied laser for pre-retinal haemorrhage on rabbits and he emphasized that for higher energy setting, the nerve-fibre of retina maybe destroyed[3]. Laser can increase the temperature of cells and it results in denaturation of proteins and collagen that leads to coagulation of tissue and it can necrotize cells. The red blood cells tend to absorb green light, hence green light laser is a good choice for diabetic eyes (Figure 1).

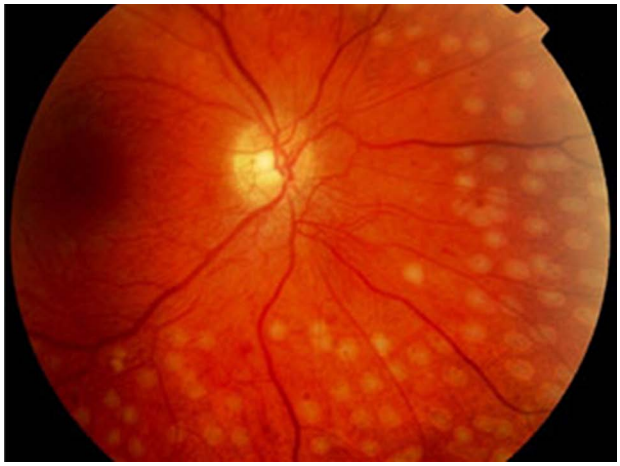

Figure 1. Coagulation of a diabetic retina by a potassium-titanyl-phosphate Neodymium-Doped Yttrium Aluminium Garnet (KDP-Nd:YAG) laser beam.

Heat effects

Increasing the body temperature leads to several effects such as hyperthermia, coagulation and other irreversible tissue effects. By increasing the temperature, the initial effect is hyperthermia. The typical range of 40-50 degrees Celsius is called hyperthermia domain within which some molecular bonds are destroyed and the membrane is altered. The reduction in enzyme activity is observed. However, the effects in this temperature range are reversible.

For temperatures around 60°C, denaturation of proteins and collagen occurs which leads to the coagulation of tissue and it can necrotize cells. Several optical treatments such as LITT and hair removal aim at temperatures above 60°C. At higher temperature the equilibrium of chemical concentration is destroyed as the permeability of membrane of cells increases.

The vaporization of water occurs at 100°C. The vaporization is sometimes referred to as the thermomechanic procedure, because within the vaporization phase, the temperature of tissue does not alter and gas bubbles are formed. The propagation of these bubbles accompanied with the alteration of their volume causes thermal decomposition of tissue

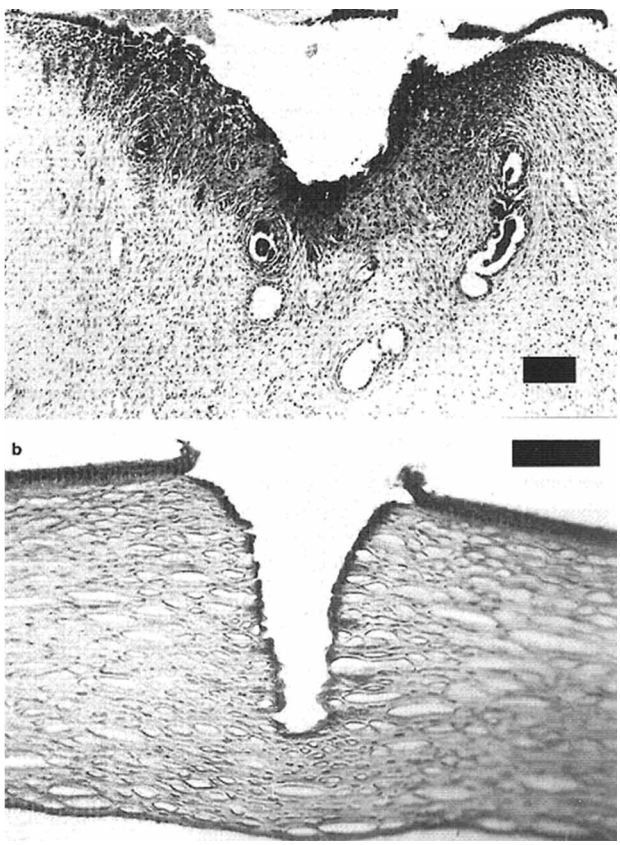

Figure 2. (a) Uterine tissue of a wistar rat coagulated with CW Nd:YAG laser(power: 10 W, bar: 80 micron) and (b) Human cornea coagulated with 120 pulses from an Erbium-Doped Yttrium Aluminum Garnet (Er:YAG) laser(pulse duration: 90 microsecond, pulse energy: 5 mJ, 1Hz, bar: 100 micron) [2].

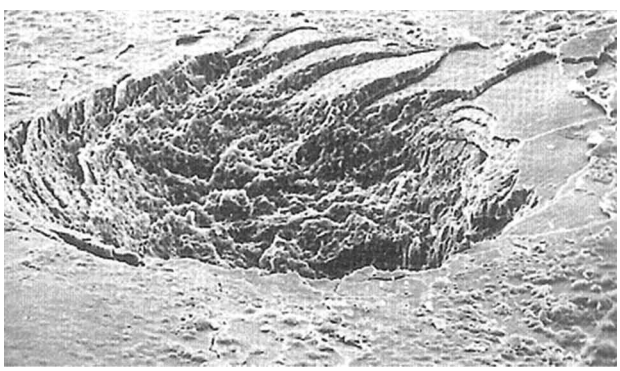

Figure 3. Human tooth vaporized with 20 pulses from an Er:YAG laser (pulse duration: 90 microsecond, pulse energy: 100 mJ, 1 Hz)[2]

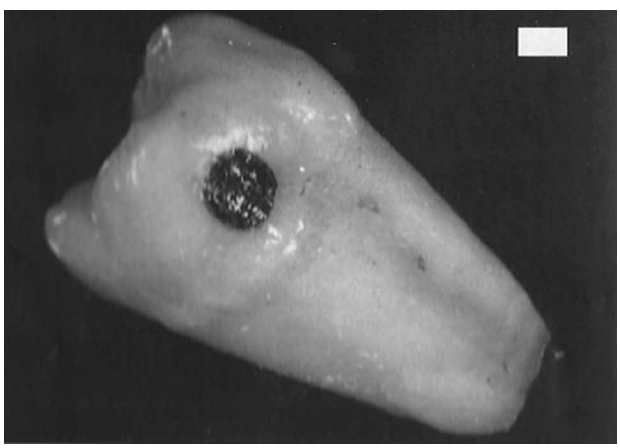

Figure 4. Human tooth carbonized with Continues-wave (CW) CO_2 laser (power 1 W, bar: 1 mm)[2].

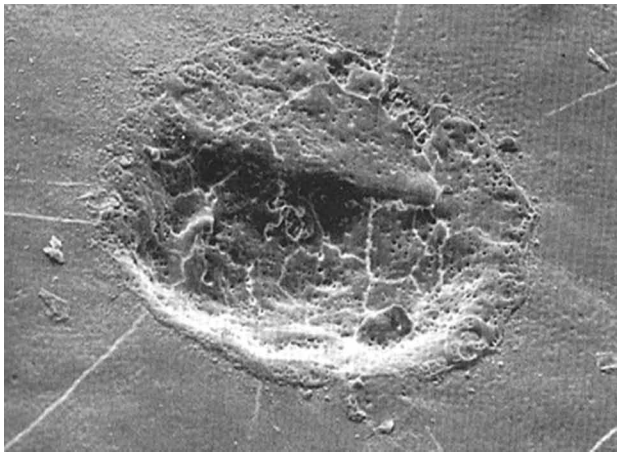

Figure 5. Human tooth melted with 100 pulses from a Ho: YAG laser (pulse duration: 3.8 microsecond, pulse energy: 18 mJ, 1 Hz)[2].

Table 1. Thermal effects of laser light for different temperatures[2].

Temperature	Biological effects
37°C	Normal
45-50°C	Hyperthermia, Reduction of enzyme activity, Cell immobility
60-80°C	Denaturation of proteins and collagen; Coagulation
100°C	Vaporization, Thermal decomposition(ablation)
>100°C	Carbonization
>300°	Melting

fragments. If all water molecules are vaporized, carbon atoms are released and the adjacent tissues are blackened and smoke rises from the skin. This stage is called carbonization (Figure 4). Finally beyond 300°C melting might occur (Figure 5). Table 1 depicts the summarized heat effects for different temperatures.

It is worth mentioning that 60°C is a critical temperature since most biological effects which occur at temperatures higher than that are irreversible.

Heat transport

The energy of laser can be absorbed by targets such as water, melanin and blood. This absorbed energy leads to a raise in the temperature of tissue. This energy can be assumed as heat energy source. The heat source, $S(r,z,t)$, inside the exposed tissue is a function of absorption coefficient a and the laser intensity $I(r,z,t)$. In this regards heat conduction and heat convection are important as they transfer the heat energy inside tissue. The physics of heat transfer is complicated; therefore we only explain some important results. One of the important parameters is relaxation time. Relaxation time is a time during which heat energy can diffuse inside tissue. The relaxation time is a function of extinction coefficient. Before we define relaxation time, the thermal penetration depth, which is another critical parameter that must be considered, shall be defined as:

$$z_{therm}(t) = \sqrt{4\kappa t} \quad (1)$$

In this equation κ is called temperature conductivity and its value is approximately the same for water $1.4\times10^{-7}\ m^2/s$ according to reference number 2. Table 2 shows the thermal penetration depth, which is defined as a distance in which the temperature decreases to 63% of its peak value. This table expresses the thermal-temporal response of water; one shall keep in mind that heat diffuses in water up to approximately 0.7 micron within 1.0 microsecond. As it was expressed in reference number 1, the penetration depth, defined as $L = 1/a$, is a distance in which the intensity of laser has decreased to 63% of its peak value[1]. Experiments show that the relaxation time (τ_{relax}) of water at the absorption peak which is for a wavelength near 3 microns is 1.0 microsecond. If the laser pulse duration τ is smaller than the relaxation time ($\tau < \tau_{relax}$), the thermal energy cannot diffuse to the penetration depth; therefore thermal effects can be negligible. Heat can be diffused up to the optical penetration depth when $\tau > \tau_{relax}$, hence thermal effects or damages are possible. The criterion $\tau_{relax} = 1\ \mu s$ is useful for wavelength of 3.0 micron, however for visible laser light τ_{relax} is larger than 270 hours! This is not extraordinary, because water is transparent for visible laser light. Relaxation time for near infra red (NIR) laser is smaller than 1.0 millisecond. One can calculate the relaxation time of different tissue by the following relation:

$$\tau_{relax} = \frac{1}{5.6\times10^{-7} a} \quad (2)$$

Because most medical applications of heat are transient, the tissue thermal diffusivity is important. In the following sections, we will introduce the important thermal parameters of biological tissues. As mentioned

Table 2. Thermal penetration depths of water [2].

Time *t*	Thermal temperature depth Z_{therm} (*t*)
1 μs	0.7 μm
10 μs	2.2 μm
100 μs	7.0 μm
1 *ms*	22.0 μm
10 *ms*	70.0 μm

Table 3. Blood perfusion rates of some human organs[2].

Tissue	Perfusion rate (ml /min g)
Fat	0.012-0.015
Muscle	0.02-0.07
Skin	0.15-0.2
Brain	0.46-1.0
Thyroid gland	~ 4.0

before, heat conduction and heat convection are important means of heat transfer. One typical example of heat conduction in tissue is the heat transfer by neighbourhood cells. The blood perfusion is an agent for heat convection; table 3 shows the perfusion rate of some human organs. It is worth stating that this perfusion rate is negligible in the first approximation, but for long exposure or LITT it has a significant role.

Heat conduction can be stated as following:

$$J = -k\nabla T \tag{3}$$

In this equation k is called heat conductivity and is expressed in units of W/mK . J is called heat flow. The value of heat conductivity at 37°C is 0.63 W/mK. According to the equation of continuity the time evaluation of heat content per unit volume $(\frac{\partial q}{\partial t})$ is determined by the divergence of the heat flow J:

$$\nabla J = -\frac{\partial q}{\partial t} \tag{4}$$

After some mathematics it is derived that:

$$\nabla^2 T(r,z,t) = -\frac{\rho c}{k}\frac{\partial T}{\partial t} + S(r,z,t) \tag{5}$$

Equation 5 is heat transfer equation. The transfer of heat in biological tissues can be modelled by this differential equation. The source term $S(r,z,t)$ contains the term of perfusion, conduction and laser source. It has been shown in the literature that the duration pulse of 1.0 microsecond is a crucial parameter and the thermal effects and hence heat transfer equation must be studied by this parameter.

For temperatures above 60°C, the necrosis can happen. To obtain the number if the remaining active cells at a certain temperature level ($C(t)$), we can use Arrhenius equation: $-\ln\frac{C(t)}{C_0} = A\int_0^t \exp\left(-\frac{e}{RT(t')}\right)dt' \equiv \Pi$ (5)

C_0 is the initial concentration of cells, A is the Arrhenius constant, e and Π are specific tissue parameters and R is the universal gas constant. The local damage of tissue can be determined by this relation:

$$\begin{aligned} -\ln\frac{C(t)}{C_0} &= \Pi \\ \frac{C_0 - C(Damage)}{C_0} &= -\exp(\Pi) \\ \frac{C(Damage)}{C_0} &= 1-\exp(\Pi) \end{aligned} \tag{6}$$

Thermography

Nowadays, the researchers look for new non-invasive biomedical imaging methods. Among biomedical imaging, thermography is a non-invasive, non-contact skin surface temperature screening technique which is cost-effective, fast and does not cause any pain on the patient[8]. It is a relatively simple imaging approach that detects the variation of temperature on the human surface.

Ammer in 1995 showed that the thermography can be used to image muscle; Low activity muscles caused by neurological deficit or by pain inhibition should result in an asymmetric thermal pattern with low temperature over non-functioning muscles. Thermograms of 50 patients with pain in one ankle joint were re-evaluated for thermal asymmetry over the lower leg. Thirty-eight patients showed a pathological side-to-side difference of temperature over the ankle joint in a range of -1.8 to 3.4 degrees. Thermal asymmetry of the anterior lower leg, defined as side-to-side difference greater than 0.5 degrees was observed in 54% of patients. Nearly all of those patients showed a decrease of temperature (mean of temperature on the affected minus temperature of the healthy side: -0.32 ± 0.78) on the symptomatic side. A similar decrease of temperature over the muscles of the anterior lower leg was found in a small group of 10 patients with palsy of the peroneal nerve. Muscular inactivity should be considered as a reason for regions of low temperature in patients with painful ankle joints[4].

Thermography is utilized in various medical fields reported in reference numbers 5-40 such as the detection of breast cancer, which is the refocus of many biomedical researchers in recent years[5-40] (Figure 6). The earliest breast thermogram was reported by Lawson[41-44]. He observed that the venous blood draining the cancer site is often warmer than its arterial supply. However, these measurements have never been confirmed by other groups and the findings might thus have been questionable. Thermograms

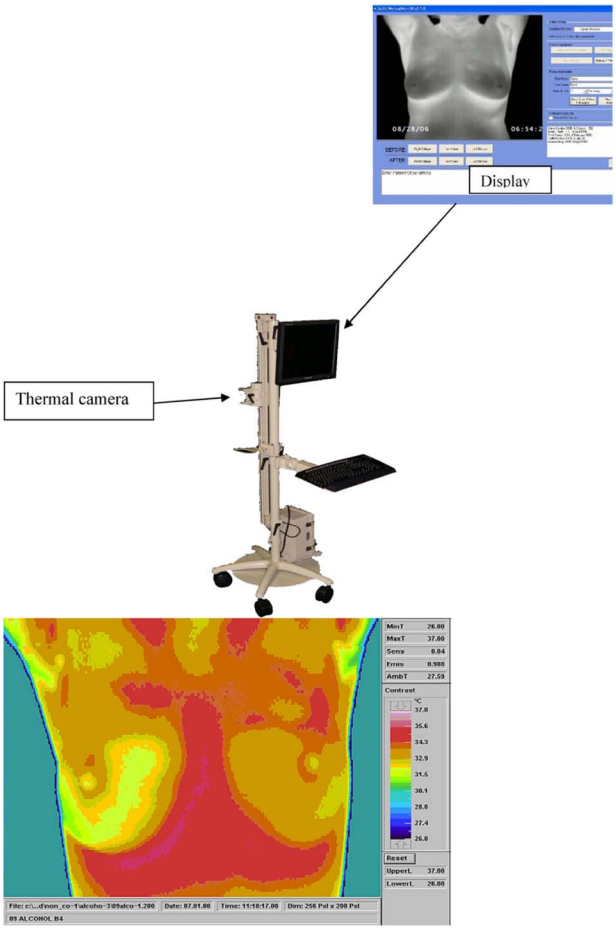

Figure 6. A thermal imaging setup for breast imaging (left picture) and Typical thermogram of an asymptomatic volunteer age 35 (right picture)[4]

alone will not be adequate for the medical practitioner to make a diagnosis. Analytical tools such as bio-statistical methods and artificial neural network are recommended to be included to study the thermogram objectively[34,45-65]. Notice that these approaches may improve the interpretation of thermal images which may lead to a higher diagnostic accuracy of infrared thermography, but these methods of analysis are not more objective than other highly accurate and precise measurement methods. With the rising use of thermal imaging, there is a need to have regulations and standards to provide accurate and consistent results. The standards are mainly based on the physics of radiation and thermoregulation of the body[4].

Figure 6 illustrates a typical thermal imaging with an asymptomatic volunteer (aged 35) thermogram. Based on mammographic examinations in 1000 Singapore women on the eve of the breast cancer awareness month -Oct. 1998[12,66], the average size of a cancerous lump[58] was 1.415 cm in spheroid shape when detected in the clinic for the first time[4]. Temperature data are extracted from the breast thermograms. The thermograms consist of many colored pixels, each representing a temperature. From the thermograms, it is possible for an experienced medical practitioner to diagnose abnormalities such as a cyst. After every pixel's temperature is compiled, bio-statistical technique can be used to treat them, such as determining the mean, median and modal temperature of the breast region[56].

Aweda showed that the Thermographic technique and energy exchange processes in 107 cancer patients were studied in order to determine relevance in cancer management[5]. The mean oxygen consumption rate in control subjects (36.13 ml/s) was higher than the mean oxygen consumption rate in breast (31.89 ml/s), head and neck (30.64 ml/s), cervical (28.05 ml/s) and other forms of cancers (30.78 ml/s). Mean metabolic heat production rate in control subjects (150.71 J/h) was higher than the mean metabolic heat production in breast (133.04Jh/h), head and neck (127.80 J/h), cervical (117.00 J/h) and other cancers (128.37 J/h). Convective rate of heat exchange was -14462.91 J/h for non-cancer persons while it was -15841.98 J/h for breast, -15509.34 J/h for head and neck, -13873.86 J/h for cervical and -3950.10 J/h for other forms of cancers. Evaporative heat loss was -10949.40 J/h for non-cancer patients, -11326.39 J/h for breast, -11229.40

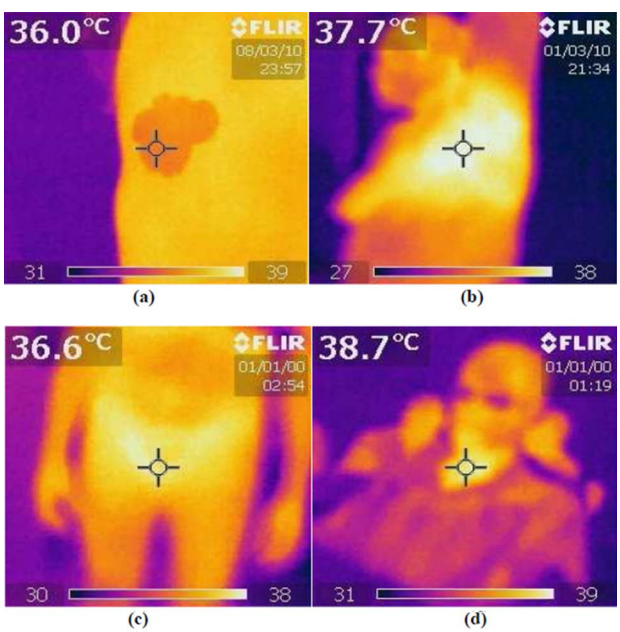

Figure 7. Typical thermographs of cancer patients: (a) is Keloid on the left arm, (b) is Cancer of the left breast post-mastectomy, (c) is the Cancer of the cervix and (d) is the Cancer of the thyroid[5].

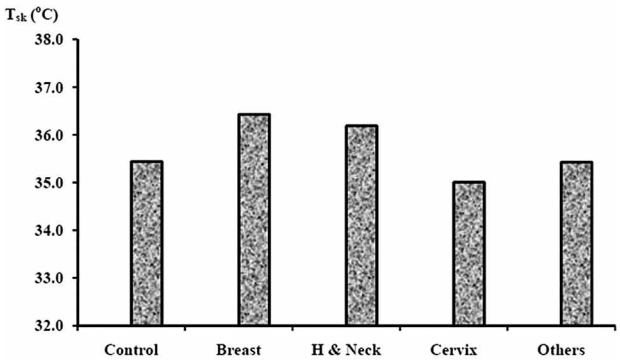

Figure 8. Mean value of skin temperature T_{sk} of cancer patient compared with control[5].

J/h for head and neck, -10788.62 J/h for cervical and -10946.63 J/h for other forms of cancers. Respirative rate of heat loss was - 6.89 J/h for non-cancer patients, - 6.08 J/h for breast, -5.85 J/h head and neck, -5.35 J/h for cervical patients and -5.87 J/h for other forms of cancers. Mean skin temperature for non-cancer patients was 35.44°C, for patients with breast cancer 36.43°C, head and neck cancer 36.19°C, cervical 35.01°C and for other forms of cancers it was 35.43°C. Figure 7 shows the aforementioned cancerous parts. The results showed that cancer patients consume less oxygen and gain heat at a higher rate than the non-cancer patients. Skin temperature combined with related physiological energy parameters could be useful in assessing and monitoring cancer patients (Figure 8 and table 4)[5].

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Table 4. Cancer distribution by site, sex, stage and skin temperature. (Continued on the next page)[5]

Cancer Type	Mean Tsk (°C)	Stage (Freq)	Male Freq (%)	Female Freq (%)	Total Freq (%)
Breast Cancer	36.34 36.48 37.52 34.92 36.49	I (5) II (16) III (6) IV (5) NS (9)	1 (0.93)	40 (37.38)	41 (38.32)
Cervix	33.70 35.93 35.89 34.73 37.70	I (1) II (4) III (7) IV (4) NS (1)	–	17 (15.89)	17 (15.89)
Head & Neck	37.83 37.12 35.28 37.04	II (3) III (5) IV (5) NS (11)	14 (13.08)	10 (9.35)	24 (22.43)
Soft tissue sarcoma	37.50 20.90 36.00	II (1) IV (2) NS (1)	2 (1.87)	2 (1.87)	4 (3.74)
Colorectal	37.10 37.40	III (1) IV (1)	1 (0.93)	1 (0.93)	2 (1.87)
Childhood	32.40 36.30	III (1) IV (1)	1 (0.93)	1 (0.93)	2 (1.87)
Anal	29.00	NS (1)	1 (0.93)	1 (0.93)	2 (1.87)
Rectal	34.60 26.40	II (1) NS (1)	1 (0.93)	2 (1.87)	3 (2.80)
Skin inclusive	35.00 35.60	II (1) NS (3)	4 (3.74)	–	4 (3.74)
Prostate	36.35 34.90 30.00 33.90	II (2) III (1) IV (1) NS (1)	5 (4.67)	–	5 (4.67)
Others	38.00 35.60 36.50	III (1) IV (1) NS (3)	2 (1.87)	3 (2.80)	5 (4.67)
Total			32 (29.88)	75 (72.88)	107 (100)

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