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A thermodynamic assessment of therapeutic hypothermia techniques

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ABSTRACT

According to literature, therapeutic hypothermia has been applied for treating conditions that causes an interruption in the delivery of oxygen to the brain, giving the patient better chances of survival with a neurological recovery and without any irreversible damage to the brain. Hypothermia is also used during surgeries and circulatory arrest. In this article, the objective temperature of hypothermia is 32 °C, which is considered mild: 32–35 °C. Three techniques of hypothermia induction were considered: external blood cooling, endovascular cooling with a catheter insertion and water bath. Energy and exergy analyses were performed to determine the clinical effectiveness of these techniques and to evaluate the best test parameters, from which it was possible to calculate the body internal temperature, destroyed exergy and exergy efficiency. Moreover, it was proposed an exergy performance index, which takes into account the ability of a given technique to change the exergy of the body. Results indicate that therapeutic hypothermia takes the subject to a state of lower destroyed exergy and higher body exergy efficiency. The exergy performance index shows that lower rates of cooling lead to a better transformation of the exergy removed from the body into variation of the body exergy.

1. Introduction

The First Law of Thermodynamics establishes that the energy must be conserved. The concept of exergy arose by combining energy and entropy balances in order to evaluate the quality of different energy conversion processes. An overall study of human body behavior requires the use of the Second Law of Thermodynamics to assess the irreversibilities of the energy conversion processes that take place in its several organs and systems.

Since the beginning of 1940, several authors tried to describe life as a function of entropy. The first attempts to use the Second Law of Thermodynamics in biological systems sought to prove Prigogine and Wiame principle [1], which states that all living organisms tend to a minimum entropy production [2–8]. Batato et al. [9] proposed a pioneer model to perform the exergy analysis to the human body. Later, Albuquerque –Neto et al. [10], Henriques et al. [11] and Mady et al. [12] applied the exergy analysis to the human body during running tests on a treadmill. Several authors [13–23] tried to correlate the points of minimum destroyed exergy with thermal comfort and thermal sensation conditions. Furthermore, the concept of entropy production and destroyed exergy were even applied in cancerous [24] and neurons [25] cells.

Regarding the thermal behavior of the human body, it can be understood as a heat engine with an optimum operating core temperature between 36 and 37 °C. An increase in the temperature can lead to a protein denaturation, and a decrease in the temperature can take to a reduction in enzymatic function. Macroscopically, these effects are identified as hyperthermia and hypothermia, respectively. It was obtained by Ref. [23] that, for high operative air temperatures and high relative humidities, the body begin to enter in a hyperthermia state.

There are two main scenarios where hypothermia plays an important role: therapeutic hypothermia (TH) [26] and hypothermia in trauma patients (HTP) [27]. Both have different classifications to sort their deepness, moreover, they have different consequences to the human body. The TH uses the benefits of reduced body temperature, whereas HTP is one of the causes of the death. A classification of therapeutic hypothermia according to the body temperature (T_{body}) was obtained from Peng and Bongard [27]:

- Mild hypothermia: $32 < T_{body} < 35$ °C.
- Moderate hypothermia: $28 < T_{body} < 32$ °C.

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Nomenclature

A	area, m^2
B	exergy rate and flow rate, W
$\mathbf{B}$	body exergy, J
b	exergy rate/flow rate per subject mass, W/kg
$\mathbf{b}$	body specific exergy, J/kg
h	specific enthalpy (kJ/kg) and heat transfer coefficient (W/(m^2K))
H	enthalpy flow rate, W
M	metabolism, W
m	body mass, kg and mass flow rate, kg/s
Q	heat transfer rate, W
r	exergy performance index, -
S	entropy rate, W/K
s	specific entropy, kJ/(kgK)
T	temperature,−°C or K
t	time, s
U	internal energy, J
w	skin wettedness, −
W	performed power, W

Greek symbols

η	efficiency, %
Φ	relative humidity, %
ω	absolute humidity, kg/kg

Subscripts and superscripts

0	thermodynamic reference
a	environment air
b	exergy
bl	blood
body	body
c	convective
dest	destroyed
e	evaporative
en	energy
env	environment
ex	expired
hyp	hypothalamus/hypothermia
in	inflow
k	index/counter
lip	lipids
M	metabolic
o	operative
out	outflow
r	radiative
mr	mean radiant
res	respiration
sk	skin
ΔT	due to body temperature variation
w	water vapor

- Severe hypothermia: $20 < T_{body} < 28$ °C.
- Profound hypothermia: $14 < T_{body} < 20$ °C.
- Deep hypothermia: $T_{body} < 14$ °C.

According to Dine and Abella [26], TH can be defined as an intentional induction body temperature to values lower than 35 °C. Behringer et al. [28] claim that mild hypothermia (32–35 °C) might be beneficial when induced during or after insults to the brain (cardiac arrest, brain trauma stroke), spinal cord (trauma), heart (myocardial infarction), and viscera (hemorrhagic shock). Furthermore, according to [26], this technique is employed for cardiac surgery or on neurosurgical procedures on the hope of protecting the brain from ischemic injury.

The main challenge in this clinical scenario is the immediate induction of mild hypothermia without producing shivering [28]. According to Dixon et al. [29], the mild hypothermia (MH) reduces the metabolic rate in approximately 7%/ °C and do not causes bradycardia. However, the exact mechanism by which TH protects against cellular and tissue injury remains unclear [26]. Nevertheless, hypothermia reduces the number of neurons lost immediately following brains ischemia and delays programmed cell death [26].

From literature analysis [26–31], it is possible to conclude that the main challenges in the studies of hypothermia as a therapy are to evaluate:

1. The most suitable technique to achieve mild hypothermia.
2. The appropriate rate of cooling and rewarming (it is established that the first should be fast and the second slow).
3. The temperature that result in better benefits to the body.
4. The duration of the test.

Moreover, there are a few articles that tried to simulate hypothermia and hyperthermia in computational thermal models of the whole body such as [31–33] and there are some authors that simulated these conditions in the brain [34]. The thermodynamic analysis may be helpful to evaluate items 1 and 2, whereas 3 and 4 are influenced by conditions that are not taken into account in the thermal models available in literature.

In this work the energy and the exergy behavior of a subject under MH (objective of body temperature around 32 °C) were analyzed. Several methods to produce hypothermia are invasive [26–31] and most tests are performed in subjects (animal or humans). The evaluation of this condition from the human thermal model proposed by Ref. [35] is a contribution to the area. Furthermore, the exergy analysis proposed in Refs. [8,12,36] is applied to three types of techniques, namely external blood cooling, catheter insertion and water bath, in order to discriminate them from the First and Second Law point of view. These techniques were chosen because, according to literature, they are more effective in not activating the shivering mechanism and, therefore, to obtain hypothermia, which is possible to evaluate using the thermal model [35]. Moreover, there are still a limited number of experimental results in animals to describe the external blood cooling and not many articles describing the whole body hypothermia in literature; this article is the first attempt to use the exergy analysis to evaluate this kind of therapy.

2. Methods

Fig. 1 indicates a schematic representation of the human body, where it is indicated the heat transfer rate and enthalpy flow rates associated with radiation (Q_r), convection (Q_c), vaporization (H_e), respiration ($\Delta H_{res} = H_{ex} - H_a$) and the performed power (W). The exergy rates associates with convection, radiation, vaporization and respiration are respectively: B_r, B_c, B_e and $\Delta B_{res} = B_{ex} - B_a$ [36].

The enthalpy flow rate associated with food intake, food wastes, water intake and urine were also taken into account. In this figure the human body is divided in two control volumes, CV1 and CV2. The first one represents the thermal and respiratory systems and the second the cellular metabolism. It is important to note that the model also takes into account the ATP (adenosine triphosphate)