ISSN XXXX XXXX © 2017 IJESC

Research Article Volume 7 Issue No.6

Flow and Temperature Control for an Innovative Hyperthermic Intraperitoneal Chemotherapy

Forum .H. Thakker[1], Prof. Sanjay .N. Patil[2]
ME Student[1], Associate Professor[2]
Department of Electronics Engineering
PVPIT, Budhgaon, Sangli, Maharashtra, India

Abstract:
HIPEC (Hyperthermic Intraperitoneal Chemotherapy) is a procedure used in cancers that are spread in the surface of the peritoneal cavity. Heated sterile solution with added chemotherapy (up to 42^0C) is circulated in the abdomen during approximately 90 minutes with the goal of killing any hidden tumor cells. It is applied directly following peritonectomy or Cytoreductive surgery. HIPEC treatment provides surgeons with the ability to apply high doses of chemotherapy directly into the peritoneal cavity without significant toxicity to the remainder of the body. The effects of the heat may increase the efficacy of the treatment. In this way the normal side effect of chemotherapy can be avoided. HIPEC treatment is used in Peritoneal Carcinomatosis. This is a broad description of a variety of tumors that present with extensive metastasis throughout the peritoneal cavity such as appendix, colon, gallbladder, ovaries, mesothelioma, pancreas, stomach and pseudomyxoma peritonei.

Keywords: Cytoreductive Surgery, Flow Control,Hyperthermic Intraperitoneal Chemotherapy (HIPEC), Peritoneal Carcinomatosis, Temperature

I. INTRODUCTION

Nowadays cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (HIPEC) represents a standard treatment for Peritoneal Carcinomatosis, a final stage of abdominal cancer. HIPEC requires the use of equipment that delivers the cytostatic solution inside the peritoneal cavity at high temperature of 41°C-43°C.

The basic of the HIPEC procedure is built on the following scientific foundations:

- An elevated body temperature, or fever (between 37.5 and 41 ^{o}C) does have a beneficial effect on the outcome of infections
- At temperatures between those of natural fevers and outright tissue destruction (between 41 and 45 ^{o}C) heat may have a natural therapeutic role because pathogens are more thermo sensitive than normal tissue
- Living tissue is susceptible to destruction by heat (generally >45^{o}C)
- Hyperthermia damages the membranes, cytoskeleton and nucleus functions of malignant cells.
- Hyperthermia causes irreversible damage to cellular perspiration of these cells. Heat at 42^{o}C also pushes cancer cells towards acidosis, which decreases the cells' viability and transplatability
- Heat is known to stimulate the immune system causing both increased production of interferon alpha and increased immune surveillance.

II. MATERIALS AND METHODS

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) allows approaching the peritoneal carcinomatosis, final stage of cancer, in a therapeutic manner.

Iulia Clitan and Vlad Muresan presented two control structures used for the temperature control in HIPEC equipment. For selected patients the treatment consists in cytoreductive surgery followed by HIPEC. The current commercially available HIPEC devices have some drawbacks, thus, Iulia Clitan and Vlad Muresan intended to develop an HIPEC equipment that surpasses the drawbacks of the existing devices, and moreover, being affordable. An important part of HIPEC device's architecture consists in a temperature control structure, since it is mandatory to deliver the cytostatic solution at a temperature of 42°C. For the temperature control, IMC controller and a neural network Model Reference Controller are used. Both controllers are based on the controlled process model. [1] Iulia Clitan and Vlad Muresan, developed fully automated HIPEC equipment that allowed a homogeneous distribution of chemotherapy drugs and heat, is able to provide optimal exposure of the patient peritoneal surface area with minimal systemic toxicity and minimal exposure of the personnel. The innovative equipment offered complex distribution system with multiple nozzles and variable flow, wireless multipoint temperature measurement system, smart control algorithms for localized flow and temperature control and the integration of the vital signs parameters monitoring to ensure patients safety. [1] Corneliu Lungoci and Ion Aurel Mironiuc presented the design of two cytostatic solution's temperature control structures, with a neural network controller and an Internal Model Control (IMC) controller. Both controller design methods use the heating process model, and in addition presented a comparison between the two control structures, from the point of view of simulated step response performance set. [2] A discrete Internal Model Controller is designed by Stroia Nicoleta and Sita Valentin for the cytostatic solution's temperature control. Due to the fact that the heating process depends on the time the solution spends inside the heating element a feedforward control structure in respect to the solution flow was also analyzed. A temperature control structure for an innovative HIPEC equipment, is under

development. [2] Santiago González-Moreno, Luis A González-Bayón, and Gloria Ortega-Pérez presented a comparison between the performances of the two control structure, via simulation. The IMC control structure is the fastest one, obtaining an improvement in the settling time of 80%. The phenomenon of cytostatic solution cooling by heat absorption by the patients was also simulated. It was noted that this control structure rejects the temperature disturbance. [3] P.H. Sugarbaker commonly used intraoperative agents mitomycin C, cisplatin, and 5-fluorouracil (5fu), used alone or in various combinations, usually administered for 30–120 minutes. For early postoperative IP chemotherapy, cell-cycle-specific drugs such as 5fu and paclitaxel are most frequently used, for up to 6 days. [3]-[8] The commercially available HIPEC devices have some shortcomings, thus Santiago González-Moreno, Luis A González-Bayón, Gloria Ortega-Pérez suggested an affordable HIPEC equipment that surpasses the drawbacks of existing devices. HIPEC equipment needs to maintain a homogenous temperature for the cytostatic solution of 42°C through the peritoneal cavity, thus, a temperature control structure is mandatory. [4] Y. Hikichi and K. Sasaki presented the design of a discrete IMC controller for the cytostatic solution's temperature control of HIPEC equipment, designed in order to overcome the operational shortcomings of the currently commercially available HIPEC devices. The adjustable filter's time constant was considered a tuning parameter and it was shown via simulation that the overshoot of the control structure's step response decreases if the value for the filter's parameter is increased. Under consideration that the most suitable controller is one that generates no overshoot and a zero steady state error. The chosen IMC controller can be implemented on an embedded processor. The phenomenon of temperature loss due to the increased solution flow was also simulated. [5] The flow rate value influences the electrical power applied to the input of the heating element, since in order to maintain a constant temperature if the flow increases one needs to modify the electrical power in order to compensate for the loss of temperature. A feed-forward control structure in respect to the flow disturbance was proposed since a feed-forward control structure can be used very successfully to improve a control loop's response to disturbances, as long as the disturbances are measurable. [5] Perhaps the most important pharmacologic rationale for combining moderate heat (42°C) and heat-augmented chemotherapy agents in the peritoneal space is drug penetration. The cytostatic solution's temperature varies with the flow of the solution, meaning, if a constant electrical power is supplied the temperature decreases with the increase of flow rate since the solution spends less time in the heater. [6] Survey suggested that Hyperthermia alone is cytotoxic at the cell and tissue levels, with formation of "heat shock" proteins. Cancerous tissues exhibit altered thermoregulation, having only a limited vasomotor response, and so massive cellular destruction occurs on prolonged exposure to heat. In addition, studies in cultured mammalian cells and in animal tumors show that hyperthermia can enhance the cytotoxicity of some chemotherapeutic agents. [7]

III. SYSTEM OVERVIEW

The flow of cytostatic solution would be controlled using a combination of feedback-feedforward control in order to obtain better control. The enhancement of temperature and flow control in terms of uniformity is done by incorporating following methodology. Figure 1 shows the basic implementation of HIPEC and the step by step procedure that takes place is as below:

1) Uniform heating using an heat exchanger

The cytostatic solution will be heated using a heat exchanger using both convection and conduction heat transfer modes. The solution will be enclosed in silicon tubing and tubing will be rolled around the exchanger fins in order to achieve uniform heating of the solution.

2) Temperature measurements at various positions

The temperature is measured at three positions to get more accurate readings.

Sensor placements:

- Outflow from heat exchanger
- Inflow in patient's peritoneal area
- Outflow from patient's peritoneal area

3) Implementation of temperature control: Set point calculation and Manipulation

The process value for temperature control will be manipulated based on the sensor readings in the loop. An PID control will be used to control the system temperature.

4) Implementation of Flow Control

The flow of the cytostatic solution is controlled by implementing feed forward control in forward loop and feedback control in feedback loop and hence achieves a tighter control.

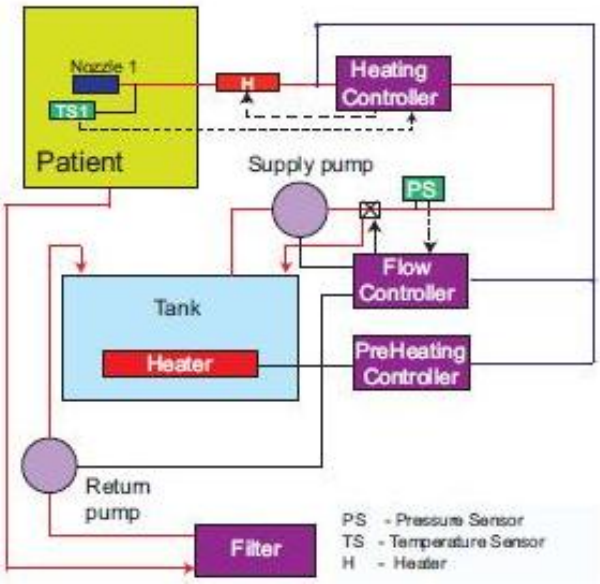

Figure.1. Implementation of hipec [2]

IV. RESULTS AND DICUSSION

There are some operational shortcomings of the currently available HIPEC equipments, like: the low number of thermal sensors that generates inappropriate distributed temperature monitoring (not allowing the thermal characterization of the entire peritoneal area); the flow distribution is uncontrolled; there are no advanced control mechanisms implemented in order to achieve homogenous temperature in the peritoneal cavity (in some cases massage of the abdomen is performed in order to homogenize the temperature in the peritoneal cavity). The objective of this work is to develop a more precise and uniform temperature and flow control for the cytostatic solution in atmosphere and in the peritoneal area. Figure 2 below shows the schematic diagram for the proposed control strategy and can overcome some of the operational shortcomings of the currently available HIPEC equipments.

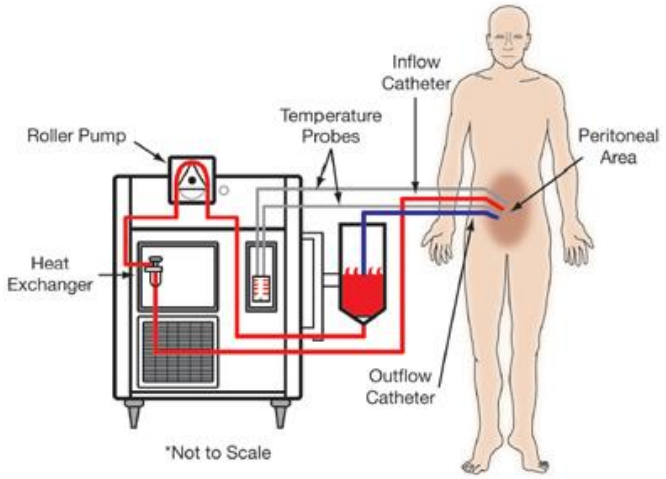

Figure. 2. schematic diagram for proposed control strategy in hipec

V. CONCLUSION

In conclusion, there is an emerging body of evidence that supports the use of HIPEC with CRS and systemic chemotherapy for primary (Stage III) and recurrence compared to CRS and chemotherapy alone. Maximal cytoreduction remains essential for overall survival rates, even when HIPEC is used. Ongoing research will further clarify the role of HIPEC for patients with advanced and recurrent cancer. The field of CRS/HIPEC has made substantial progress over the past several decades. Developments in this area will likely continue to complement ongoing advances in systemic therapies; indications for and observed outcomes of surgery will change as the understanding and treatment approaches of tumors develop. Most importantly, the field should remain committed to embracing new knowledge through rigorous scientific study. Peritoneal surface malignancy remains to date a challenging clinical program, but ongoing and evolving multidisciplinary approaches, including CRS/HIPEC for selected patients, have provided new optimism for treating patients with historically few options.

VI. REFERENCES

[1]. Iulia Clitan, Vlad Muresan, Mihail Abrudean, Daniel Moga and Honoriu Valean, Corneliu Lungoci and Ion Aurel Mironiuc, "*Flow and Temperature Control for an Innovative Hyperthermic Intraperitoneal Chemotherapy Equipment"* in 19th International Conference on System Theory, Control and Computing (ICSTCC), October 14-16, 2015 Cheile Gradistei, Romania

[2]. Clitan Iulia, Moga Daniel, Muresan Vlad, Stroia Nicoleta, Sita Valentin, Lungoci Corneliu and Mironiuc Ion Aurel, "Design of a Temperature Controller for an Hyperthermic Intraperitoneal Chemotherapy Equipment" at 10th Jubilee IEEE International Symposium on Applied Computational Intelligence and Informatics May 21-23, 2015 Timişoara, Romania

[3]. P.H. Sugarbaker, "Cytoreductive surgery plus hyperthermic perioperative chemotherapy for selected patients with peritoneal metastases from colorectal cancer: a new standard of care or an experimental approach?" in Gastroenterol. Res. Pract., 2012.

[4]. S. González-Moreno, L. González-Bayón, and G. Ortega-Pérez, "Hyperthermic intraperitoneal chemotherapy: Rationale and technique" World J Gastrointest Oncol, vol. 2, no. 2, pp. 68-75, 2010.

[5]. Y. Hikichi, K. Sasaki, R. Tanaka, H. Shibasaki, K. Kawaguchi and Y.Ishida, "A discrete PID control system using predictors and an observer for the influence if a time delay", In: International journal of modeling and optimization, vol. 3, no. 1, 2013, pp. 1-4.

[6]. S. Van Ruth, R. Mathôt, R.W. Sparidans, J.H. Beijnen and V.J. Verwaal, "Zoetmulder F a N. Population pharma cokinetics and pharmacodynamics of mitomycin during intraoperative hyperthermic intraperitoneal chemotherapy", in Clin. Pharmacokinet.,vol. 43, no. 2, 2004, pp. 131-143. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14748621.

[7]. F. Mohamed ,T. Cecil , B. Moran, and P. Sugarbaker "A new standard of care for the management of peritoneal surface malignancy" Available at: http://www.ncbi.n lm.nih.gov/ pmc/articles/PMC3070715/

[8]. Y.R. Huo, A. Richards, W. Liauw, D.L. Morris "Hyperthermic intraperitoneal chemotherapy (HIPEC) and cytoreductive surgery (CRS) in ovarian cancer:A systematic review and meta-analysis" Available online at www.sciencedirect.com and published with www.ejso.com