

# Hemicolectomy With Concomitant Heated Intraperitoneal Chemotherapy: A Case Study

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**Abstract:** The use of heated intraperitoneal chemotherapy is an emerging new adjunct in the treatment of adenocarcinoma of the colon. However, documentation regarding perfusion circuitry and techniques associated with this therapy remain largely undescribed. After consultation with the surgical service team, a custom designed circuit was constructed for this procedure. Institutional approval and informed consent were obtained for surgical debulking and heated intraperitoneal chemotherapy for a 58-year old female. After surgical resection, a right hemicolectomy was performed and pathological specimens obtained. A modified custom circuit using a roller pump was first primed with 3 liters of Dianeal® PD-2 and recirculated until temperature of 41°C was obtained. The circuit was then connected to the patient for infusion of perfusate via Blake drains placed in the deep

pelvis. Two additional drains were placed in the subdiaphragmatic space for return. Perfusate containing 30 mg of Mitomycin-C was circulated at 600–800 mL/min for 60 min at 41°C. An additional 10 mg of Mitomycin-C was then administered through the circuit for an additional hour under similar conditions. Upon completion, a washout procedure was performed with 2 additional liters of Dianeal® PD-2. The patient tolerated the procedure well and was discharged postoperative day 7. We describe the successful use of a perfusion-administered heated intraperitoneal chemotherapy regimen as an integral part of successful treatment of adenocarcinoma of the colon. **Keywords:** Mitomycin-C, hemicolectomy, HIPC, perfusion circuitry, colon cancer. *JECT. 2005; 37:75–78*

Despite current advances, cancer continues to be a significant cause of mortality in the United States. Our most recent data suggests that more than 1.4 million new cases of cancer are reported annually, attributing to 23% of all reported deaths in the year 2000; making it second only to cardiovascular disease (1,2). In terms of economic cost to the nation, the National Cancer Institute, a component of the National Institute of Health, requested a record budget for fiscal year 2004 of 6.2 billion dollars to support its efforts in conducting cancer research, education and training (1).

Among all cancer types, colon cancer comprised approximately 15% of all diagnoses in the United States in

2000, effecting approximately 93,800 individuals (1). In the same year, a total of 48,570 individuals lost their battle against this deadly disease (1). Further statistical facts are equally cause for concern. Estimates place the overall lifetime risk of developing colon cancer at 6% for the general population (1). After the age of 40, the risk increases and, on average, colon cancer prematurely shortens one's lifespan by an average of 13.4 years (1). Colon cancer patients typically are given a poor prognosis, with the median survival time estimated at 5–6 months after diagnosis (1,3,4).

Despite these grim statistics, however, the development of innovative new treatment regimens, surgical techniques, and technology have steadily increased 5-year survival rates from 41% in 1950–1954 to 63% in 1992–1999 (1). Novel treatment regimens include multiple routes of administration of chemotherapeutic medications, timing of treatments, and the use of heated intraperitoneal chemotherapy (HIPC) (2–5). Surgical techniques incorporating “no touch isolation techniques” (5) prevent the wide-

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spread dissemination of tumor cells. Technology-related advances include improved colon cancer screening and detection methodologies (6) and a better understanding of the pharmacokinetics of chemotherapy treatments. The focus of this investigation, heated intraperitoneal chemotherapy or HIPC, is one of the more promising resources in our arsenal against colon cancer.

The use of HIPC is a reemerging adjunct in the treatment of colon cancer, as reports utilizing techniques similar to HIPC have been reported for many years in surgical literature (2,5). Renewed interest in this technique stems from several factors including better understanding of patient selection criteria, chemotherapeutic advances, and continuing research (2–5).

The successfulness of HIPC as a treatment regimen is the result of a hyperthermic synergy between the chemotherapeutic agent and delivery method (6–8). Experimentally it has been demonstrated that hyperthermia alone is cytotoxic to malignancies and decreases the interstitial pressure of the tumor mass, allowing for improved drug penetration (6–8). Additionally, heating the chemotherapeutic agents in HIPC creates a synergistic heat/drug effect, increasing the cytotoxicity of selected chemotherapeutic agents such as Mitomycin-C, at the peritoneal surfaces (6–8).

The application of HIPC, although widely described, frequently lacks sufficient detailed descriptions of extracorporeal circuit design. Our task was to then develop a system from the available literature for the conduct of HIPC without a universal template in which to follow.

The subject of this case report is a 58-year-old female with right colon adenocarcinoma with carcinomatosis requiring surgical debulking. A major concern of our surgical team was that debulking the tumor singularly may allow free floating remnants of the carcinoma to become seeded within the peritoneal cavity (4,5). The addition of HIPC to surgical debulking was felt to provide the best chance of ensuring that the surgical margins and inevitable free-floating remnants of cancer within the peritoneal cavity were not reseeded. Because of the patient's young age, lack of significant comorbidity, and the demonstrated potential for an improved statistical outcome, the decision was made to use HIPC in conjunction with surgical debulking. Upon consulting with the surgical team, the circuit design used in this technique report was developed to infuse heated chemotherapeutic agents to the patients' peritoneal cavity.

## DESCRIPTION

### Circuit Design

The set-up and technique for this HIPC procedure was accomplished with a team approach to the problem. The design of our perfusion delivery system was developed to

incorporate the single-use disposable products and extracorporeal circulation components common to most perfusion departments (Figure 1). The delivery system used consisted of a base console with a roller pump (Medtronic Inc., Minneapolis, MN) for transfusing the intraperitoneal chemotherapeutic fluid, and a modified heater/cooler (Terumo/Sarns, Ann Arbor, MI) for regulating and maintaining perfusate temperature at 41°C. Modification of the heater/cooler unit was necessary to achieve chemotherapy infusion solution temperatures in excess of the factory limits placed on the unit. The circuit consisted of two cardiectomy reservoirs (Medtronic Inc.), a cardioplegia heat exchanger (Medtronic Inc.) with temperature monitoring site, and 3/8-inch and 1/4-inch polyvinyl chloride (PVC) tubing (Medtronic Inc.).

### Technique

Upon completion of the surgical debulking process, cannulation for HIPC drug delivery was accomplished with the placement of four 24-French closed suction Blake™ drains (Ethicon Inc., Somerville, NJ) placed in the peritoneal cavity. Two of the drains were placed in the deep pelvis for infusion of the perfusate, and two drains were placed in the subdiaphragmatic space to reclaim the heated perfusate for recirculation. A disposable temperature probe for continuous monitoring was then placed within the peritoneal cavity (Medtronic Inc.). The surgical incision necessary for debulking the tumor was then temporarily closed with a running monofilament suture (Ethicon Inc.), and additional temperature probes were placed near the cannula inflow and outflow sites on the surface of

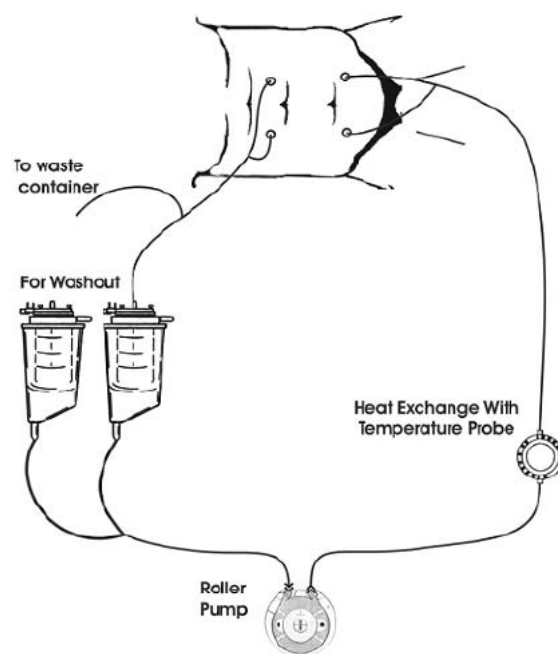


Figure 1. Diagram of circuit.

the skin (Medtronic Inc.). Priming of the system was accomplished with the addition of 3 liters of Dianeal® PD-2 (1.5% Dextrose) peritoneal dialysate (Baxter Healthcare, McGaw Park, IL) to the delivery cardiectomy located on the right in the circuit diagram. Dianeal® PD-2 was chosen as a chemotherapeutic carrier fluid due to its balanced electrolyte composition. The dialysate (PD-2) was recirculated within the pump circuit (prime prewarm) for a period of approximately 15 minutes to prewarm it to a temperature of 43°C (Table 1). The dialysate alone was then circulated within the patients' closed peritoneal cavity for a period of 30 minutes and brought to a temperature of 41°C. Heater/cooler water-bath temperatures were varied from 40–44°C to achieve the peritoneal cavity temperature of 41°C.

To facilitate adequate gravity drainage once HIPC was begun, it was necessary to raise the patient table to its fullest height, and included a minimal degree of "reverse Trendelenberg" angle. This method of delivery assures maximal contact of the heated chemotherapeutic agent to the target area of the colon and surrounding margins. Once a target temperature of 41°C was reached, 30 mg of Mitomycin-C (Roche, Indianapolis, IN) was administered into a nonfiltered port on the same cardiectomy. The Mitomycin-C containing perfusate was then allowed to circulate throughout the peritoneal cavity for 60 minutes at pump flows of approximately 600–800 mL/min and 41°C. After 60 minutes of treatment, an additional ten mg of Mitomycin-C was added to the perfusate and further circulated for an additional 60 minutes under identical conditions. As a guide, the fluid level in the cardiectomy was monitored as an indication of the amount of perfusate returning from the peritoneal cavity. Upon conclusion of the chemotherapeutic recirculation, a washout procedure was performed using the second cardiectomy, which contained 2 liters of heated Dianeal® PD-2 alone. This washout solution was diverted to a chemical waste container after the leaving the peritoneal cavity, and disposed of in a manner consistent with hospital policy.

## COMMENT

The benefits of HIPC therapy are self-evident when evaluating survival rates of individuals treated and those untreated. Currently, the 2-year survival rate after treatment is approximately 45–60%, with a 5-year survival as

high as 30% when HIPC is used in combination with surgical debulking (2–5). This is a dramatic increase when considering the median survival time for untreated colon cancer is estimated at 5 to 6 months after diagnosis.

Indications for use of HIPC in gastrointestinal cancer patients are dynamic and evolving. As this treatment modality continues to gain acceptance, a larger number of patients will likely benefit. The list of therapeutic advantages of HIPC include many of which were the primary criteria for its use in our patient, including the probability of positive margins after resection, and the potential for peritoneal seeding of cancer cells after surgical resection. Chemotherapeutic advances continue to make great strides as well. Mitomycin-C was chosen as our chemotherapeutic agent due to its long-standing successfulness in treating adenocarcinomas (2,4,6) through a mechanism that exerts a cytotoxic activity by forming cross-links between strands of DNA, inhibiting DNA synthesis in rapidly proliferating cancerous tissue (2,4,6). Although this disruption of DNA synthesis is advantageous in the treatment of cancer, it is important to note that it is indiscriminate in its global effects on other body tissues. Therefore, the use of HIPC is not without risk, and advocates of this technique report side effects similar to those of administration of chemotherapeutic agents alone (2,4). Although the advantages greatly outweigh the disadvantages of using this therapy, these side effects should not be overlooked in the postoperative care of these patients. Common side effects can include anemia, atelectasis, pleural effusions, elevation of liver enzymes, leukopenia, renal insufficiency, and thrombocytopenia (2,4,9). Anticipation of these side effects, and prompt treatment, serve to lessen the impact of these post-treatment complications.

Our efforts to develop a suitable HIPC delivery circuit are presented in this technique description as a model by which others may further refine and develop. By incorporating components available to most perfusion departments, this treatment can be performed in a safe and consistent manner.

In summary, no one will contest the fact that cancer of the colon still remains a formidable disease process that continues to be a significant source of morbidity and mortality in the United States. We believe HIPC is a promising and welcome adjunct in the fight against this deadly disease. As this technique becomes more widely used, a more uniform standard of application and circuitry will evolve for the benefit of these individuals.

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**Table 1.** Agent circulation amounts and times.

|               | Time (min) | Flow (mL/min) | Agent           | Temperature |
|---------------|------------|---------------|-----------------|-------------|
| Prime prewarm | 15         | 2000          | Dianeal PD-2    | 43°C        |
| Prep          | 0–30       | 3000          | Dianeal PD-2    | 41°C        |
| Treatment     | 30–90      | 600–800       | Mitomycin 30 mg | 41°C        |
| Treatment     | 90–150     | 600–800       | Mitomycin 10 mg | 41°C        |
| Wash          | 150–180    | 600–800       | Dianeal PD-2    | 41°C        |

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