

# ***Closed hyperthermic intraperitoneal chemotherapy with open abdomen: a novel technique to reduce exposure of the surgical team to chemotherapy drugs***

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## **Abstract**

**Exposure of the surgical team to toxic drugs during hyperthermic intraperitoneal chemotherapy (HIPEC) remains a matter of great concern. In closed-abdomen HIPEC operating room staffs are not exposed to drugs, but the distribution of the heated liquid within the abdomen is not optimal. In open-abdomen HIPEC, the opposite is true. Even though the open-abdomen method is potentially more effective, it has not become a standard procedure because of the risk of exposure of members of the team to drugs.**

**We present a new technique (closed HIPEC with open abdomen) which ensures protection against potentially contaminating exposure to liquids, vapours and aerosols, and allows permanent access to the whole abdominal cavity.**

**Its principle is to extend the abdominal surgical wound upwards with a sort of “glove-box”. The cutaneous edges of the laparotomy are stapled to a latex «wall expander». The expander is draped over a special L-section metal frame placed above the abdomen. A transparent cover containing a « hand-access » port like those used in laparoscopic surgery is fixed inside the frame.**

**In 10 patients, this device proved to be hermetic both for liquids and vapours. Intra-abdominal temperature was maintained between 42 and 43°C during most of the procedure. The whole abdominal cavity was accessible to the surgeon allowing optimal exposure of all peritoneal surfaces.**

**This technique allows optimal HIPEC while limiting the potential toxic effects for the surgical, medical and paramedical teams.**

**Author Keywords** Peritoneal carcinomatosis ; colorectal cancer ; hyperthermic intraperitoneal chemotherapy ; toxic effects ; mutagenicity

**MESH Keywords** Abdominal Cavity ; Body Temperature ; Chemotherapy, Cancer, Regional Perfusion ; instrumentation ; methods ; Colorectal Neoplasms ; pathology ; Combined Modality Therapy ; Digestive System Surgical Procedures ; Humans ; Hyperthermia, Induced ; Laparoscopy ; Occupational Diseases ; prevention & control ; Operating Rooms ; Patient Care Team ; Peritoneal Neoplasms ; drug therapy ; secondary ; surgery ; Pseudomyxoma Peritonei ; surgery

## **INTRODUCTION**

Hyperthermic intraperitoneal chemotherapy (HIPEC) with surgical cytoreduction may increase survival in patients with colorectal peritoneal carcinomatosis; survival at 5 years is around 30% in selected patients [1 , 2 ]. With its progressive expansion [3 ], the use of chemotherapy in the operating room raises the problem of the safety of people present in the operating room. This danger remains a matter of great concern that could limit the expansion of this otherwise beneficial technique.

The toxic and teratogenic effects of these drugs have been established experimentally, but the effects on people handling them remain controversial [4 ]. As well as the risk of local and general toxic effects, professional exposure may induce obstetrical risks and an increased probability of cancer [5 , 6 ].

There are two types of HIPEC: one in which the abdomen is closed during chemotherapy (closed-abdomen HIPEC) and another one in which the abdomen is left open (open-abdomen HIPEC). The most common open-abdomen technique is the « coliseum technique » as described by Sugarbaker: the cutaneous edges of the surgical wound are lifted upwards and suspended by threads from a frame positioned horizontally above the abdomen [7 ]. The frame can be partially covered by a plastic sheet but spillage and emanation of vapours can not be totally controlled. Moreover, aerosols may form [8 ]. The closed-abdomen procedure avoids exposure to the chemotherapy drugs but the distribution of the heated liquid is not uniform, preferential circuits exist and some peritoneal surfaces are underexposed to chemotherapy.

We have designed a novel HIPEC technique, « open-closed », which combines the advantages of the two techniques, both open-abdomen and closed-abdomen: optimal exposure of the patient, minimal exposure of the staff to chemotherapy drugs.

## **SURGICAL TECHNIQUE**

The principle is to prolong the abdominal cavity by a sort of glove-box extending from the edges of the surgical wound. After surgical cytoreduction, HIPEC is prepared. The surgeon cuts a hole in the middle of a sheet of latex (expander for HIPEC, TP10000-Landanger, France), which has the same shape and size of the surgical wound. The edges of the hole are hermetically fixed to the cutaneous edges of the laparotomy using staples very close together (Figure 1 ). Temperature probes (one for the diaphragm and one in the pelvis) pass through the latex sheet, as well as inflow and outflow. Two vertical supports and two horizontal arms of a Thompson retractor (TH00300, Landanger, France) are fixed to the operating table. A special metallic frame (hexagonal, « L » section) is fixed in a horizontal position to the two arms, 20 cm above the abdomen. The expander is pulled upwards through the centre of the frame. The tip of the outflow catheter is positioned between the right lobe of the liver and the diaphragm in order to prevent a suction effect on hollow viscera during HIPEC. The tip of the inflow catheter is positioned against the inside face of the expander. A metacrylate transparent cover with a 12-cm-diameter central opening (Protection Lid, TP40000, Landanger, France), is smeared with an anti-fog solution. A « Gelport ®» (TP41000, Landanger, France), is installed in the central opening of the cover. The cover is inserted inside the frame and the latex expander serves as a seal. Closing forceps (TP42000, Landanger, France) fix the apparatus (Figure 2 ). The operator wears extra-long gloves (TP20080, Landanger, France) with lubricant and must make sure that all abdominal peritoneal surfaces are accessible to his/her hand.

The abdominal cavity is then filled with 2L/m<sup>2</sup> of dialysis solution at 37°C. The pumps are switched on and the liquid is heated. As soon as the temperature reaches 41.5°C the antimetabolic drug is added to the circuit. For colon tumours and pseudo-myxomas, 20 mg/m<sup>2</sup> of mitomycin C are given initially, and then 5 mg/m<sup>2</sup> after 30 minutes; the total duration of the HIPEC is one hour. The intra-abdominal temperature is maintained between 42 and 43° C throughout the procedure. Temperature can be brought down by reducing the inflow rate. The homogeneity of the temperature is ensured by constant stirring of the liquid with sequential opening of the different abdominal spaces, and by moving the tip of the inflow drain or tilting the table, according to the temperature gradient between the diaphragm and the pelvis ( Figure 3 ). The non-submerged edges of the surgical wound are regularly bathed with the liquid. Once the HIPEC is finished, the liquid is sucked out and the abdominal cavity washed. The skin is incised a few millimetres outside its junction with the expander and both are removed en bloc.

## RESULTS

Nine patients with colon peritoneal carcinomatosis and one with pseudomyxoma have been treated using this technique. Setting up the apparatus (expander, frame and cover) never took more than 30 minutes. Intra-abdominal hyperthermia of 41.5°C was obtained in less than 15 minutes and a temperature between 42 and 43°C was maintained during most of the procedure. All abdominal spaces were accessible.

Visibility through the cover was sufficient throughout the procedure allowing safe control of the viscera, inflow and outflow at every moment. There were no fluid leaks along the staples line fixing the expander to the skin.

## DISCUSSION

Most cytotoxic substances have shown a carcinogenic, teratogenic and/or mutagenic effect in experimental studies. Cases of skin irritation, ulcers and even necrosis have been reported following the use of these drugs [4 ]. Mitomycin-C, the most widely used agent in HIPEC, has been classified as a possible carcinogen by the International Agency for Research on Cancer [9 ]. Platinum and its derivatives may cause flushes, dizziness and anaphylaxis [10 ]. Three studies have reported a significant increase in the number of miscarriages or congenital malformation in health-care personnel exposed to antineoplastic drugs [11 –13 ]. Five studies have shown significant increases in the mutagenicity of urine in nurses working in oncology departments, but techniques used to detect cytogenetic effects or chromosomal aberrations are neither specific, nor sensitive and no formal conclusions can be drawn [14 –19 ]. Most authors recommend great caution when handling these substances [13 ]. It must be underlined that most of these studies concerned personnel who handled these drugs in centralised units, according to very strict regulations and under laminar-flow hoods. Open-abdomen HIPEC exposes operating room personnel to the potential risk of contamination by chemotherapy drugs through the skin but also through the respiratory, digestive and ocular systems (spills, splashes, aerosols, barrier defects in the gloves or contact with vapours present in the surrounding air when the liquid is heated) [6 , 20 ]. Protection offered by standard surgical masks has been discussed [21 , 22 ]. Eyes-itching is often reported by the staff during open HIPEC.

This risk is the main obstacle to the generalisation of the open-abdomen technique; in Europe, many teams perform closed-abdomen HIPEC exclusively for safety reasons. There is undeniably a feeling of insecurity.

Recent studies concerning open-abdomen HIPEC did not find mitomycin-C either in the operating room atmosphere or in the urine of the operating personnel. However, the methods of these studies were not optimal and there was a lack of statistical power [20 , 22 , 23 ]. Moreover, their results did not reassure surgical teams (not even the authors), as the resulting recommendations were: to exclude from HIPEC teams pregnant women or those wishing to conceive, as well as those breast-feeding, or with a history of miscarriage; to exclude

all people with a history of oncologic or immunosuppressant therapy or with antecedents of haematological disease; to maintain positive pressure in the operating room; to use double impermeable gloves, goggles, FFP3 masks, HEPA filters and extraction hoods [24 ]; and to perform a medical check-up for the personnel every 6 months.

Closed-abdomen HIPEC is theoretically less satisfactory from a therapeutic point of view as the liquid follows preferential circuits between the inflow and outflow catheter [8 ]. Some peritoneal surfaces (mesentery, small bowel and retrogastric area) are underexposed to the heated liquid. We abandoned the closed-abdomen technique after a small number of procedures for this reason [25 ]. In open-abdomen HIPEC, the liquid can be stirred permanently allowing better temperature homogeneity, better diffusion of the liquid and delivery of the drugs.

Only a closed system allowing an homogeneous distribution of chemotherapy drugs and heat would provide optimal exposure of the patient with minimal exposure of the personnel. Certain teams use plastic sheets or a rigid enclosure positioned above the abdomen; neither of these systems is really effective nor reproducible [26 , 27 ]. Sugarbaker's coliseum technique can not protect accurately against splashes, aerosols and vapours.

Our « glove-blox » ensures minimal exposure of the personnel; but not zero, in so far as despite being wiped by the gelpport, traces of the liquid remain on the glove after withdrawal of the hand from the abdomen. Following HIPEC, certain surgical acts (possible digestive anastomosis, setting up drains, parietal closure) are performed once the glove-box has been removed; the aim of washing the abdominal cavity before removing the cover is to reduce exposure of the personnel during this final phase.

There is no leakage of the liquid at the joint between the expander and the skin provided that the staples are placed at very close intervals. In so far as the expander prolongs the edges of the surgical wound, the parietal margins can be bathed in the liquid: this is impossible using Fujimura's expander, which covers the parietal margins [27 ].

Catheters and probes do not pass through the abdominal wall before the HIPEC, thus avoiding also the risk of tumour recurrence in the wall. The abdomen is filled with 2 L/m<sup>2</sup> of liquid making possible to obtain an adequate concentration of drugs. With such a volume, the whole of the abdominal cavity will be sufficiently filled in provided that the expander is not pulled too tight, which would increase the volume of the cavity. From a subjective point of view, the staff's perception of HIPEC has totally changed: the general feeling of insecurity has disappeared.

Total additional cost (1400 euros for the disposable kit and 2300 euros for the metallic frame adapted to the Thompson retractor) seems acceptable given the potential advantages in terms of safety on the one hand and the overall cost of classical open-abdomen HIPEC on the other (calculated at 39358 euros by Elias et al.) [28 ]. Setting-up and dismantling times are also acceptable, given the average duration this surgery, which is approximately 8 hours [29 ]. Latex allergy is the only contraindication to the use of this device.

Previous experimental studies in rats conducted by our group suggested that the closed-abdomen technique may increase penetration of the drugs into the tissue thanks to a higher pressure, but this has not been proved in humans [30 ]. If a higher pressure were found to improve penetration of drugs, this could also be achieved using the closed open-abdomen technique described here.

This technique combines the advantages of both open and closed-abdomen HIPEC: optimal exposure of the patient with minimal exposure of the surgical team to antineoplastic drugs. Regarding the risks associated with handling chemotherapy agents, Favier [6 ] wrote: « There will be always doubts, and these should benefit those concerned through a continual search for ways to minimize contact by adapting procedures ».

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### Figure 1

A hole with the same shape size of the laparotomy is cut in a large sheet of latex with round extremities to avoid angles. The edges of the hole are hermetically fixed to the skin with staples (every 5mm).



**Figure 2**

A transparent cover containing a gel port in its middle is fixed on the frame sustained by the Thompson retractor. It closes hermetically the expanded abdominal cavity. Temperature probes, inflow and outflow pass through the latex sheet. Homogeneity of the temperature and the exposure of peritoneum in the abdomen is ensured by permanent stirring of the liquid and by repositioning the inflow catheter or tilting the operating table.



**Figure 3**

Transverse schema showing the expanded abdominal cavity during hyperthermic intraperitoneal chemotherapy.

