

Peer Review File

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Reviewer A

I have read and reviewed with interest the manuscript entitled “Intra-Abdominal Temperature Variation During Hyperthermic Intraperitoneal Chemotherapy Evaluated via Computational Fluid Dynamics Modeling”. Given the paucity of evidence in this topic, I think is of interest to publish different scientific views on the topic, and I see yours as one of them. Nonetheless, I have several very important comments I would like the authors to address, for clarity, and to understand limitations and new knowledge created with this.

We are grateful to the reviewer for the kind assessment.

Major comment 1: After reading the manuscript, it is not clear to me whether any heat transfer is modeled. This needs to be very clear to the readers because a big issue here is heat transfer. If there is heat transfer, then many other considerations need to be made, including the countercurrent effect of the great vessels in the posterior abdominal cavity (aorta, cava), the abdominal wall and organs outside the peritoneal cavity, and finally the transfer of heat outside the abdominal region.

Reply 1: We agree with the reviewer. Heat transfer within the cavity was modeled using Ansys Fluent’s energy equations, which we now describe in the Supplementary Material. This simulation did not simulate heat transfer to the environment outside of the patient. The reviewer is correct in that other aspects of heat transfer could be considered, including heat transfer to the outside environment as well as effects of heat transfer of vasculature. These refinements will be considered in future work.

Changes in the text:

- The Supplementary Material has been updated with a new section titled “Model of Heat Transport”.
- The “Initial and Boundary Conditions” section in the main manuscript (Materials and Methods) has been updated (Page 10, Line 207-213): “To represent a slight decrease in temperature normally found in anesthetized patients (38), body fluid within the cavity and organs were set to 309.15 K (36°C). Inlet fluid temperature was set to 316.15 K (43°C). Based on prior studies, target tissue temperature was set at 39°C (39). Heat transfer to and from the catheters was assumed to be negligible in this study and was not modeled. The abdominal cavity was treated as the boundary of the system with a Dirichlet boundary condition of 309.15 K. All other initial condition settings were left at default values.”
- The Discussion has been updated (Page 18, Line 368-372) to clarify, “The effects of heat transfer from the abdomen to the exterior, fluid flow in vasculature, and organs surrounding the abdominal cavity, including the thoracic cavity and pelvic bones, will also be considered in future work. Thermal heterogeneity would likely be increased due to gravitational forces and additional organs”.

Major comment 2: It appears to me that you have modeled flow in a simplified peritoneal cavity and used temperature to explain zones where the flow may imply inadequate temperature distribution. Is this correct? Now, you need to discuss why your probe 2 (and probe 3 for reverse flow at 1120) was consistently different than the other ones. Is it the geometry that you chose? Since your organs are rigid, you need to explain how this result may be useful for future research or how it potentially could relate to clinical practice.

Reply 2: The reviewer raises an excellent point. For this iteration of the model, the fluid simulation software treated the abdominal cavity and the organs as rigid objects. In constructing the model, we emphasized the importance of creating reasonable approximations of at-risk areas within the abdomen. However, increasing the fidelity of this model is expected to refine results and may lead to additional findings. It is unclear how this would impact the current findings. It is possible that softening the organs will reduce the resistance to flow and thereby decrease the variance found across the different test conditions. It is also possible that allowing organs to collapse down on each other, as occurs in vivo, may exacerbate areas of poor flow resulting in even more exaggerated flow or temperature variance. This latter possibility is consistent with published findings that smaller perfusion volumes lead to inefficient flow and clearance of HIPEC fluid (van der Speeten et al., *Cancer Chemother Pharmacol.* 2011;68(1):147-56).

Out of the seven locations of clinical interest, the location of Probe 3 (next to duodenum) was the closest location to the inlet catheters during forward fluid flow. In addition, the mesentery of the large bowel isolated Probe 3 from reverse flow. Consequently, greater differences were observed in the velocity and temperature between forward and reverse flow directions. On the other hand, Probe 2 (inferior to small bowel mesentery), being secluded from fluid flow by the TCM, experienced a low fluid velocity for all flow cases. We note that these results are consistent with Wong et al. (*Pleura Peritoneum.* 2022;7(2):95-102), who found that tumors on the small bowel were associated with decreased HIPEC efficacy after cytoreductive surgery.

Changes in the text:

The Discussion has been updated (Page 18, Line 375-380): “The anatomy of the 3D abdominal cavity and organs, especially the small bowel, was simplified for these simulations and may affect the temperature distribution. Despite this simplification, the results of this study are consistent with (53), which found that HIPEC efficacy decreased and was associated with decreased survival when peritoneal tumors were located on the small bowel. Future 3D cavity and organ design could be informed by anthropometric data and patient-specific CT scans to investigate interpatient heterogeneity and to personalize model predictions.”

The Results have been updated (Page 14, Line 291-295): “Probe 2, being secluded from fluid flow by the TCM, experienced a low fluid velocity for all flow cases (<0.001 m/s). Due to its proximity to inlets during forward flow and the large bowel mesentery relative to other probe locations, velocity magnitude at Probe 3 (next to duodenum) under forward flow trended higher than with reverse flow.”

The Discussion in discussing limitations also states (Page 18, Line 363-365): “Abdominal organs are known to behave viscoelastically (32), which may affect fluid flow and, by extension, heat distribution in the abdominal cavity. It is unclear, however, whether non-rigid organs would improve or impede the fluid flow and associated heat transport at at-risk locations.”

Major comment 3: Previous research had already shown that temperature distribution is heterogeneous. This is both clinically and in simulation. How does your research add to the existent knowledge, or what is important that we can learn other than “temperature is heterogeneous”. You need to focus more on this so that the paper can have more value, otherwise is just another attempt at simulating flow.

Reply 3: We greatly appreciate the reviewer’s feedback. This study tested the hypothesis that fluid flow dynamics at specific intra-abdominal locations at-risk of inadequate drug and temperature exposure could be evaluated via a computational fluid dynamics (CFD) model of closed-technique HIPEC fluid flow in a human abdominal cavity, with the goal to enable protocol optimization. To the best of our knowledge, a CFD platform for at-risk locationspecific

evaluation of HIPEC has not been previously evaluated.

Changes in the text:

The Abstract (Page 2, Line 36-43) states: “Although studies have focused on clinical outcomes, the flow dynamics at specific intra-abdominal locations at-risk of harboring malignant cells remain poorly understood but are likely to impact the drug pharmacokinetics. Consequently, optimal protocols remain uncertain, with efficacy critically dependent on drug temperature and flow rate. This study tested the hypothesis that fluid flow dynamics at specific at-risk locations could be evaluated via a computational fluid dynamics (CFD) model of closed HIPEC in a simulated human abdominal cavity, with the goal to enable protocol optimization.”

Major comment 4: You explain that the initial fluid was set to 309.15 K(36°C). This is one of my main concerns because I do not understand this:

1.) The HIPEC time itself does not start until the difference in temperatures between inflow and outflow is 1-2 degrees maximum. Are you then showing what happens during the initial stabilization period, before chemo is added?

Reply 4.1: The reviewer raises an important question. The initial fluid temperature at 309.15 K was for the body fluid already residing within the abdominal cavity. Based on prior studies, target tissue temperature was set at 39°C (Kusamura et al., 2008). This temperature is reached for most of the tissue locations on average within ~30 min, which falls within the 90-min length of the simulated procedure, and follows the clinical protocol at our institution.

Changes in the text:

The “Initial and Boundary Conditions” section in the main manuscript (Materials and Methods) has also been updated (Page 10, Line 207-210): “To represent a slight decrease in temperature normally found in anesthetized patients (38), body fluid within the cavity and organs were set to 309.15 K (36°C). Inlet fluid temperature was set to 316.15 K (43°C). Based on prior studies, target tissue temperature was set at 39°C (39).”

Results: A new Table 1 has been added to the manuscript to report the time to reach the target temperature.

2.) Even if the organs were at 36, the outflow fluid is higher than that because it entered the cavity at 43C, can you explain?

Reply 4.2: The reviewer is correct. The intra-abdominal temperatures increased due to heat transfer during the procedure lasting 90 min due to the inflow at 316.15 K. This heat transfer model is now described in Supplement as noted in Major Comment 1. We found that the outlet temperature may not reflect the temperature at the intra-abdominal locations of clinical interest. The outlet fluid increased in temperature during the procedure but lagged the maximum average temperatures at the individual probe locations.

Changes in the text:

Results: The new Table 1 added to the manuscript shows that the outflow temperature may not necessarily reflect the temperatures at the at-risk locations within the abdomen.

3.) I do not see where the changes of the outflow temperature are depicted over time to understand if this simulation could be used.

Reply 4.3: We have updated the manuscript to address this concern. The results suggest that the outflow temperature may not necessarily reflect the temperatures at the intra-abdominal at-risk locations.

Changes in the text:

Abstract (Page 3, Line 59-61): “The results further suggest that monitoring outflow temperature may be inadequate for assessing HIPEC performance at at-risk locations.”

Results (Page 13, Line 273-275): “In contrast, the outflow did not necessarily reflect the

conditions at the probes, reaching 311.65 ± 0.18 K by 90 min for all the configurations tested.”
Discussion (Page 19-20, Line 408-410): “The results further suggest that monitoring outflow temperature may be inadequate for assessing HIPEC performance. Without intra-abdominal temperature monitoring of at-risk locations, it may not be feasible to determine whether target temperatures and temperature homogeneity are being achieved.”

Other Comments:

1. Line 14. I suggest: “...heated drug solutions via catheters inserted into the peritoneal space”.

Reply 1: We thank the reviewer and have changed the text accordingly.

Changes in the text (Page 2, Line 34-36): “Hyperthermic intraperitoneal chemotherapy (HIPEC) targets intraperitoneal tumors with heated drug solutions via catheters inserted into the peritoneal space.”

2. Line 16. “Gauge targeting efficacy”. I do not understand this sentence very well. Can you rephrase?

Reply 2: We thank the reviewer and have updated the text.

Changes in the text (Page 2, Line 36-40): “Although studies have focused on clinical outcomes, the flow dynamics at specific intra-abdominal locations at-risk of harboring malignant cells remain poorly understood but are likely to impact the drug pharmacokinetics. Consequently, optimal protocols remain uncertain, with efficacy critically dependent on drug temperature and flow rate.”

3. Line 30. Your conclusion needs to be consistent with the results. The current sentence is not a conclusion.

Reply 3: We agree with the reviewer and have updated the Conclusion.

Changes in the text (Page 3, Line 62-67): “Without intra-abdominal temperature monitoring at at-risk locations, it may be unfeasible to determine whether target temperatures and temperature homogeneity is being achieved during HIPEC. This work demonstrates that computational analysis offers the capability to monitor intra-abdominal locations at-risk of suboptimal heating and fluid flow given specific HIPEC parameters, and represents a first step towards designing efficacious tumor targeting during HIPEC.”

4. Line 62. “during the duration”...please rephrase. Does not read well.

Reply 4: We thank the reviewer and have updated the text.

Changes in the text (Page 6, Line 102-104): “Regardless of approach, it is critical for the success of HIPEC that the peritoneal surfaces be exposed equally at elevated temperatures over the course of the procedure”

5. Overall the introduction seems too long. I think the authors should concentrate in the issue at hand, which is how to understand flow dynamics and its impact on the distribution of drug and temperature in the peritoneal cavity.

Reply 5: We agree with the reviewer and have revised the Introduction.

Changes in the text (Pages 4-5): Removed text at Lines 74-80, 82-83, 86-89, 97-103.

6. Lines 92-93. Do you have a reference for the checklist?

Reply 6: We thank the reviewer and have added the reference.

Changes in the text (Page 7, Line 142-143): “This article is presented in accordance with the

MDAR (Materials Design Analysis Reporting) checklist (28)”

7. Line 97. I believe you meant "...To represent a human intrabdominal cavity undergoing HIPEC", because you are not representing the entire body at all.

Reply 7: **The reviewer is correct. The text has been updated accordingly.**

Changes in the text (Pages 8, Line 147): **"To represent a human intra-abdominal cavity undergoing HIPEC"**

8. Line 97 to 99 can be split into 2 or more sentences because the current one is too long.

Reply 8: **We agree with the reviewer and have updated the text.**

Changes in the text (Page 8, Line 147-152): **The text has been split into two sentences.**

9. Line 116. Importantly, you would need to acknowledge in the limitations that your catheter set up is not completely realistic because the catheters often extend deep into the cavity. Often, the inflow catheters extend posteriorly, and outflow may only be anterior.

Reply 9: **The reviewer is correct that the catheter placement can be variable. The placement was specified by the practice at our institution and was consistent with HIPEC during minimally invasive surgery. For example, in (Ba et al., 2024), both inflow and outflow were anterior to the patient.**

Changes in the text:

Discussion has been updated to state (Page 18, Line 365-367): "The catheter inflow and outflow were limited in this study to the anterior of the abdominal cavity; other configurations may be evaluated in future work."

10. Line 142. "...found to better replicate blood flow patterns than laminar" please rephrase, I do not understand this very well.

Reply 10: **We agree with the reviewer and have updated the text.**

Changes in the text (Page 10, Line 193-194): **"SST $k-\omega$ has also been found to better replicate blood flow patterns than laminar flow models."**

Figures:

Figure 3, why are the temperature changes depicted from minute 20? Can you explain?

Reply: **We thank the reviewer for noting this oversight. The figure has been updated to show the temperature changes from the initial time.**

Changes in the text (Page 28): **Updated Figure 2 is now included.**

Reviewer B

Major remarks:

The pelvis had been forgotten from the model? any reason that I can understand

Reply 1: **We thank the reviewer for this question. We chose to simulate a simplified abdominal cavity whose contour mimics a human pelvis. The bone structure was not modeled but will be considered in future work.**

Changes in the text:

Discussion has been updated (Page 18, Line 368-370): "The effects of heat transfer from the abdomen to the exterior, fluid flow in vasculature, and organs surrounding the abdominal cavity, including the thoracic cavity and pelvic bones, will also be considered in future work"

Reading the paper is very difficult – by example only with the abstract

The abstract is poorly informative: it is impossible to understand if

i) the process is a mathematical study using in silico model for fluid evaluation, or in vivo process using big animal model as pigs, or human detection during real HIPEC procedure. Because reading the sentence: “This study tested the hypothesis that fluid flow dynamics at specific intra-abdominal locations of clinical interest could be evaluated via computational fluid dynamics modelling”; I can understand that the study is a validation using computational model compared with human HIPEC obtained results.

Reply 2: We are grateful to the reviewer for this feedback. The manuscript has been revised in various places to improve readability. In particular, the sentence noted in the Abstract has been reworded.

Changes in the text:

Sentence in Abstract has been updated (Page 2, Line 40-43): “This study tested the hypothesis that fluid flow dynamics at specific at-risk locations could be evaluated via a computational fluid dynamics (CFD) model of closed HIPEC in a simulated human abdominal cavity, with the goal to enable protocol optimization.”

ii) HIPEC could be performed using open or close procedure, it is necessary to decide wish one is used

The introduction explains advantages and difficulty related with the two procedures, that is correct. But no information on that in the abstract.

Reply 3: We agree with the reviewer and have updated the Abstract accordingly.

Changes in the text:

Abstract has been updated (Page 2, Line 40-43): “This study tested the hypothesis that fluid flow dynamics at specific at-risk locations could be evaluated via a computational fluid dynamics (CFD) model of closed HIPEC in a simulated human abdominal cavity, with the goal to enable protocol optimization.”

iii) Some HIPEC machine use one pump resulting in one flow with two catheters (entrance and outflow) but some used two pump, with double number of catheter and sure a better spatial distribution

Reply 4: The reviewer is correct. This study used two catheters located in the upper abdomen and two catheters located in the lower abdomen, following the practice at our institution.

Changes in the text:

Abstract (Page 2, Line 46-48) has been updated: “The cavity was subjected to forward (superior to inferior flow) or reverse flow directions at 800 cc/min or 1120 cc/min through four catheters, two as inlets and two as outlets, placed in upper and lower abdominal positions”

iv) There is no result on the abstract section? By example what is the maximal temperature difference between two place?

Reply 5: The reviewer raises an important issue. The maximum temperature difference from the initial condition to simulation end (t = 90 min) was 3.6 K at the probe next to the duodenum.

Changes in the text:

Abstract has been updated (Page 2, Line 54-56) to state: “Temperature and fluid flow over the course of 90 min respectively varied from 0.93 K and <0.001 m/s inferior to small bowel mesentery (800 cc/min forward flow) to 3.6 K and 0.01 m/s next to the duodenum (either 800 cc/min or 1120 cc/min forward flow).”

Abstract has been further updated (Page 3, Line 59-61): “The results further suggest that monitoring outflow temperature may be inadequate for assessing HIPEC performance at at-risk

locations.”

Results has also been updated (Page 14, Line 280-283): “The largest difference between temperature and fluid flow was between Probe 2 under 800 cc/min forward flow configuration (0.93 K and 1E-5 m/s) and Probe 3 (3.6 K and 0.01 m/s) under both 800 cc/min and 1120 cc/min in forward flow (Figure 5C).”

Result section is very hard to understand – please delete part of the result and synthesize.

Reply 6: We thank the reviewer for this feedback. The Results section has been revised. The Results statement in the Abstract has also been updated as noted above.

Changes in the text:

Results section has been extensively revised. Text has also been deleted as described in Reply 7 below.

Minor comment:

The volume in litre of the fluid and the abdominal cavity had to be reported, in the abstract. Some comments are reported in the result section and had to be deleted, and reported in the discussion section.

Reply 7: The reviewer is correct, and the volume of the cavity and fluid therein is now reported in liters. The comments reported in Results section have been removed.

Changes in the text:

Abstract (Page 2, Line 44-34): “A computer-aided-design (CAD) model of a human intraperitoneal cavity (30 L) was coupled with computational fluid dynamics analysis.”

Abstract (Page 2, Line 46-34): “The cavity was subjected to forward (superior to inferior flow) or reverse flow directions at 800 cc/min or 1120 cc/min through four catheters, two as inlets and two as outlets, placed in upper and lower abdominal positions (net fluid volume: 18.5 L).”

Methods (Page 8, Line 147-149): “To represent a human intra-abdominal cavity undergoing HIPEC, an abdominal intraperitoneal space (volume: 30 L) was designed in SOLIDWORKS (V.2021, Dassault Systèmes, Waltham, MA), software for 3D computer-aided design (CAD).”

Methods (Page 8, Line 155-159): “Because chemotherapeutics in HIPEC, such as cisplatin (29), are commonly diluted in a water-based solution such as 1.5% dextrose isotonic peritoneal dialysis solution or saline (30, 31), water was chosen as the simulated fluid. Accordingly, the cavity was modeled as an enclosure filled with water (net fluid volume: 18.5 L) assumed to contain rigid, unmovable organs.”

Following text has been removed from Results:

(Page 12, Line 240-243): “With forward flow, temperature change at the probes stabilized by 90 minutes in both 800 cc/min (Figure 3A) and 1120 cc/min (Figure 3B) cases. Temperature change was also relatively constant by 90 minutes for reverse flow simulations regardless of flow rate (800 cc/min, Figure 3C, and 1120 cc/min, Figure 3D).”

(Page 14, Line 295-296): “Velocity magnitude at probe 3 (next to duodenum) under forward flow trended higher than with reverse flow.”

(Page 156 Line 330-333): “More generally, at least 60 different HIPEC protocols have been identified in literature across 135 journal articles, with many articles partially reporting or omitting HIPEC parameters. Consequently, the current HIPEC landscape is a challenge for CFD validation but provides an opportunity for CFD-derived refinements of the HIPEC design.”

HIPEC is used to describe a treatment performed in the surgical field, during surgery. If the procedure is done after, without general anaesthesia, you have to use another word.

Without flow we call that EPIC, with a flow please find a word, or use nonsurgical-HIPEC ?

Reply 8: The reviewer is correct. This model is intended to simulate a patient that has been put under general anesthesia and has undergone cytoreductive surgery in the abdomen. With the abdomen sutured, a closed HIPEC procedure is then simulated to target any residual tumor cells. Changes in the text:

Introduction (Page 76, Line 137-139) states: “This study implements a CFD model to simulate the flow of solution within the abdominal cavity during closed HIPEC, enabling evaluation of fluid flow dynamics at specific at-risk locations.”

Line 252: More generally, at least 60 different HIPEC protocols have been identified in literature across 135 journal articles, with many articles partially reporting or omitting 254 HIPEC parameters (9).

The different publication did not report HIPEC technical aspect, because everyone known what type of procedure is performed regarding past publication, so stop the discussion using that, it is untrue – same regarding the lack of analysis to the temperature and flow, that had been done 25 years ago – I can send you some pictures if necessary ...

Reply 9: We agree with the reviewer and have removed the statement. The intent is to convey that variations of HIPEC in clinical practice make it challenging to predict efficacy of the procedure.

Changes in the text:

Introduction (Page 7, Line 109-120): “While studies have established concepts such as synergism between chemotherapy and hyperthermia (12) and the degree of tumor tissue penetration (13), relatively little is understood about how flow influences temperature homogeneity and drug distribution. Recent literature highlights that HIPEC efficacy remains controversial, due in part to variation of key cycle parameters in clinical practice (14-16), including temperature, volume, flow rate, and duration. A comprehensive understanding of these parameters is a prerequisite to developing a standardized high-quality HIPEC technique.”

Results (Page 16, Line 130-133): Removed the text: “More generally, at least 60 different HIPEC protocols have been identified in literature across 135 journal articles, with many articles partially reporting or omitting HIPEC parameters (9). Consequently, the current HIPEC landscape is a challenge for CFD validation but provides an opportunity for CFD-derived refinements of the HIPEC design.”

Figure: more than using a number for probe 1, 2, 3 - give in the legend what is it? pelvis? stomach?

Reply 10: The reviewer raises an important point. The explanation of the numbers has now been included in the figure caption.

Changes in the text:

Legend for Figure 2 (Page 25, Line 467-469): “Probe locations; 1: between small and large bowels; 2: inferior to small bowel mesentery; 3: next to duodenum; 4: superior to liver; 5: superior to fundus; 6; posterior to stomach; 7: posterior to liver.”

to conclude for a publication

I'm really not convince by the work - majority of result is probe 2 and in a human practice we did not have a high recurrence rate at that place, rally not.

Reply 10: We greatly appreciate the reviewer's feedback and have revised the manuscript accordingly. This study tested the hypothesis that fluid flow dynamics at specific at-risk locations could be evaluated via a computational fluid dynamics (CFD) model of closed HIPEC in a simulated human abdominal cavity, with the goal to enable protocol optimization.

For this iteration of the model, the fluid simulation software treated the abdominal cavity and the organs as rigid objects. In constructing the model, we emphasized the importance of creating reasonable approximations of at-risk areas within the abdomen. However, increasing the fidelity of this model is expected to refine results and may lead to additional findings. It is unclear how this would impact the current findings. It is possible that softening the organs will reduce the resistance to flow and thereby decrease the variance found across the different test conditions. It is also possible that allowing organs to collapse down on each other, as occurs in vivo, may exacerbate areas of poor flow resulting in even more exaggerated flow or temperature variance. This latter possibility is consistent with published findings that smaller perfusion volumes lead to inefficient flow and clearance of HIPEC fluid (van der Speeten et al., *Cancer Chemother Pharmacol.* 2011;68(1):147-56).

Out of the seven locations of clinical interest, the location of Probe 3 (next to duodenum) was the closest location to the inlet catheters during forward fluid flow. In addition, the mesentery of the large bowel isolated Probe 3 from reverse flow. Consequently, greater differences were observed in the velocity and temperature between forward and reverse flow directions. On the other hand, Probe 2 (inferior to small bowel mesentery), being secluded from fluid flow by the TCM, experienced a low fluid velocity for all flow cases. We note that these results are consistent with Wong et al. (*Pleura Peritoneum.* 2022;7(2):95-102), who found that tumors on the small bowel were associated with decreased HIPEC efficacy after cytoreductive surgery.

Changes in the text:

The Abstract has been updated (Page 2, Line 40-43): “This study tested the hypothesis that fluid flow dynamics at specific at-risk locations could be evaluated via a computational fluid dynamics (CFD) model of closed HIPEC in a simulated human abdominal cavity, with the goal to enable protocol optimization.”

The Results have been updated (Page 14, Line 291-295): “Probe 2, being secluded from fluid flow by the TCM, experienced a low fluid velocity for all flow cases (<0.001 m/s). Due to its proximity to inlets during forward flow and the large bowel mesentery relative to other probe locations, velocity magnitude at Probe 3 (next to duodenum) under forward flow trended higher than with reverse flow.”

The Discussion has been updated (Page 18, Line 375-380): “The anatomy of the 3D abdominal cavity and organs, especially the small bowel, was simplified for these simulations and may affect the temperature distribution. Despite this simplification, the results of this study are consistent with (53), which found that HIPEC efficacy decreased and was associated with decreased survival when peritoneal tumors were located on the small bowel. Future 3D cavity and organ design could be informed by anthropometric data and patient-specific CT scans to investigate interpatient heterogeneity and to personalize model predictions.”

The Discussion in discussing limitations also states (Page 18, Line 363-364): “Abdominal organs are known to behave viscoelastically (32), which may affect fluid flow and, by extension, heat distribution in the abdominal cavity.”