Dear Editor:

We would like to thank you and the reviewer's for their expertise and time commitment necessary to the review our manuscript. Reviewer's #503243 and #502871 had no recommendations for manuscript modification. However, Reviewer #58388 provided us with several constructive comments. We have made a concerted effort to address the reviewer's concerns. We are also willing to make further modifications, if necessary.

Reviewer #58388 Comments: The authors should better defined what they call hypoxic cholangiopathy? This is very important as they report a rate of intrahepatic cholangiopathy that is so far the worst in the literature. Did they include any bile duct complications, including the simple anastomotic stricture?

- **Authors' Response:** We have changed common bile duct/intrahepatic duct necrosis to "common bile duct and intrahepatic duct necrosis. HC was diagnosed by endoscopic retrograde cholangiogram (ERC) or percutaneous transhepatic cholangiogram (if ERCP was performed with inability to traverse roux limb), and simple anastomotic strictures were excluded from the analysis. These changes were made to the materials and methods section, page 6, second paragraph.

Reviewer # 58388 Comments: Despite this high rate of intrahepatic cholangiopathy, the retransplantation rate and the graft survival is quite acceptable. This is quite strange. Maybe the authors perform protocol MRI to all patients, explaining why 50% of patients were considered as developing cholangiopathy? With such bad results, did the authors decide to change their policy of acceptance of DCD livers?

- **Authors' Response:** At the University of Colorado protocol MRI's were not performed. If DCD liver recipients had persistent elevated alkaline phosphatase and total bilirubin these patients underwent an ERCP and/or PTC. If the cholangiogram showed common bile duct with intrahepatic duct necrosis or common bile duct and intrahepatic duct necrosis these patients were stented and/or retransplanted. The recipients who were amenable to stent placement would have right and left hepatic duct stents placed. These were then changed every 4 – 8 weeks or sooner depending on their symptoms (i.e. worsening pruritis or cholangitis). Due to aggressive post operative management, in conjunction with our GI and IR teams, our graft survival and retransplantation rates are acceptable. Furthermore, moving forward ("Era 3") we have become as

selective as Era 1 and have started using tissue plasminogen activator (TPA) through the hepatic artery upon reperfusion of the hepatic veins and portal vein as demonstrated by the University of Toronto transplant team. We have added this to the discussion along with the reference, page 21, end of first paragraph.

Reviewer # 58388 Comments: even if the authors performed 45 DCD LTx, they exclude from further analysis one patient who died per-operatively. When calculating the rate of ischemic cholangiopathy, this case should also be excluded. The authors should describe 50% of ischemic cholangiopathy rather than 48.9% (22/44); All data should be corrected in such a way.

- **Authors' Response:** The patient who was excluded from the analysis died intra-operatively. According to the tables, Table 2 – n=44, Table 3 – n=43 (not all data points were present in 1 recipient and therefore that recipient was excluded), Table 4 – n=44, Table 5 – n=45 (the patient who died was included in this analysis because the liver was sewn in prior to the intraoperative death), Table 6 – n=44. We have made changes to the methods section, page 6, end of second paragraph. We have also made changes to the results section page 10, first paragraph. The 1, 3, 5 year patient and graft survival rates were correctly calculated.

Reviewer # 58388 Comments: In their paper the authors described a more liberal acceptance criteria in the second part of their experience. These acceptance criteria of the 2 different periods should be explained and compared. To my view, there criteria seem quite strict even in the second period. A recent paper published in Br J Surg suggested even the use of DCD liver grafts from donors over 70y of age, but with a very short CIT. - Was there a change of surgeons (increased CIT, increased suture time) in the second period? This could explain the problem the authors report. The procurement total WIT is not very long (22 min) even in the second period.

- **Authors' Response:** We demonstrate different era's to show that era 2 represented a nearly 3 fold increase in DCD livers performed compared to era 1. Because our HC outcomes were equivalent too or better than national outcomes for DCD livers during era 1, we began to utilize more liberal selection criteria for era 2. With this being said, in the United States, about 6500 deceased donor liver transplants are performed each year. Of the 6500 about 300 donation after circulatory death liver transplants are performed each year. .

- Neither longer warm nor cold ischemic times were related to HC in era 2. Please see discussion page 21, end of first paragraph.

Reviewer # 58388 Comments: The liver transplant procedures should be better explained. By pass or no bypass? Portal or arterial reperfusion?

- **Authors' Response:** The University of Colorado Transplant team abandoned venovenous in 1995. Therefore, all recipient liver transplants during this time period were performed off bypass. Warm ischemic time was the time out of ice to reperfusion of the hepatic veins and portal vein. This has been added to the Methods section page 8, first paragraph.

Reviewer # 58388 Comments: Were the procurements performed by less experienced surgeons in the second era (longer time between aortic perfusion and liver in ice)?

- **Authors' Response:** We have added asystole-to-cross clamp times to Table 6. These times were similar and statistically insignificant between era 1 and era 2. We did not evaluate cross clamp time to liver in ice time. We will add this to the limitations section, page 21. However, being that aystole-to-cross clamp times were similar, likely explantation of the donor liver would yield similar results. A direct relationship was observed with longer recipient warm ischemic times in era 2, compared to era 1, however this did not correlate with recipient HC. This was added to the discussion, page 21, first paragraph.