Evaluation of liver regeneration in human after portal vein embolization and partial hepatectomy using in vivo ^{1}H decoupled - ^{31}P magnetic resonance spectroscopy imaging

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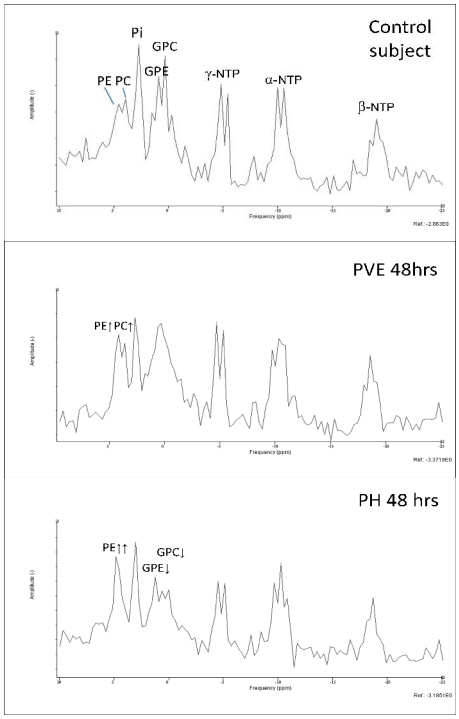
Objectives: Portal vein embolization (PVE) has been proved to be an efficient procedure to increase liver volume before major liver resection in colorectal (CRC) liver metastases patients [(1)]. At our institution, one population which commonly undergoes PVE prior to liver resection for metastatic CRC is the group that has had prior extensive chemotherapy which can generate changes in the liver parenchyma. Most studies considered PVE a similar injury as partial hepatectomy (PH) to stimulate liver regeneration. However, given the fact that the embolized lobe is still present after PVE and that arterial flow changes are different after PVE vs. PH, some have postulated that the process of regeneration after liver PVE and PH might be different [(2,3)]. The present study compares the metabolic features of hepatic regeneration induced by PVE and PH using in vivo ^{1}H decoupled - ^{31}P MRSI.

Methods: ^{31}P MRSI data were acquired from the livers of healthy subjects (control, n=8), left liver lobe of patients at 48 hours after right PVE procedure (PVE 48 hrs, n=6) and remnant liver of patients at 48 hours following PH (PH 48 hrs, n=4). In the PVE population, all patients had undergone prior combination chemotherapy which included 5FU or FuDR combined with oxaliplatin and or irinotecan. In the PH population, one patient had no prior chemotherapy, 2 had only 5FU and one had 5FU+ irinotecan. All investigations were performed on a 1.5 Tesla Signa scanner equipped with a stand-alone proton decoupler. ^{31}P MRSI data were acquired using a dual ^{1}H-^{31}P coil pair (Medical Advances) and a pulse-and-acquire sequence with Waltz-4 decoupling and low level CW power to maintain NOE. Phosphoethanolamine (PE), phosphocholine (PC), Phosphomonoester (PME), inorganic phosphate (Pi), glycerophosphoethanolamine (GPE), glycerophosphocholine (GPC), glycerophosphorylethanolamine (PDE) and nucleoside triphosphates (NTP) were quantitatively analyzed from all subjects. Metabolite levels corrected for coil sensitivity and saturation (normalized unit, n.u.) and peak area ratios were compared in three groups (Table 1).



Results: Liver ^{31}P MRS acquired from a normal control subject, a PVE 48 hr patient and a PH 48 hr patient were shown in the figure. A slight increase in PE and PC was noted at PVE 48 hrs. At 48 hours after PH, PE is highly elevated and the PDE region appears reduced. Results for individual metabolite quantities and metabolite ratios are shown in Table 1. **PVE 48 vs. PVE baseline:** There was a trend toward increased PME, PME/PDE, PME/NTP and decreased PDE at PVE 48 hrs compared to their own baseline values (data not shown) but only the change of PME/PDE was significant. This could be due to 1) a relatively slow, weak response to PVE as the regeneration compared to PH or 2) effect of prior chemotherapy on the liver parenchyma. **PVE 48 vs. PH 48 vs. normal controls:** At 48 hours, PME/NTP in PH was slightly higher than PVE but this was not significant. The PME/NTP value in PH 48 was significantly higher than controls. This suggests the presence of liver cell membrane synthesis and cell proliferation during hepatic regeneration. However, more extensive changes were seen in the PH 48 group including higher PME/PDE, PE/NTP, and PE/PC ratios and lower PC/NTP values compared to those at PVE 48 hrs and normal control subjects, possibly indicating that phospholipid turnover was more rapid at 48 hrs after PH than those after PVE procedure. PDE/NTP was higher in PVE 48 hrs because it started from a greater baseline value possibly due to an effect of multiple tumor presence in liver parenchyma or prior chemo-agent exposure in this patient group. No significant difference was observed in NTP/Pi ratio among control, PVE and PH subjects.

Conclusion: ^{31}P MRS is a valid technique to noninvasively evaluate the cell membrane metabolism during hepatic regeneration. The different pattern of biochemical changes following PH and PVE indicated that the early hepatic regeneration process after PVE is not as strong as it is after PH.

References: 1. Jaeck D, et al. Am J Surg 2003; 185: 221-9. 2. Lee KC, et al. World J Surg 1993; 17: 109-15. 3. Tashiro S. J Hepatobiliary Pancreat Surg 2009; 16: 292-9

Table 1: comparison of phosphorus metabolites (n.u.) and peak ratios among control subjects and patients at PVE 48 hrs and PH 48 hrs.

Subjects	PME	PDE	NTP	PME/PDE	PME/NTP	PDE/NTP	PE/NTP	PC/NTP	NTP/Pi	PE/PC
Control (n=8)	6.47 ± 1.93	23.92 ± 6.86	4.28 ± 1.32	0.52 ± 0.15	1.02 ± 0.27	2.06 ± 0.50	0.53 ± 0.22	0.45 ± 0.13	0.93 ± 0.33	1.20 ± 0.43
PVE 48hrs (n=6)	7.22 ± 1.18	25.01 ± 8.27	3.35 ± 0.65	0.51 ± 0.13	1.37 ± 0.35	2.67 ± 0.38#	0.55 ± 0.38	0.66 ± 0.14	0.86 ± 0.24	1.02 ± 0.17
PH 48hrs (n=4)	7.85 ± 2.57	13.32 ± 5.91	4.72 ± 1.74	0.97 ± 0.25*	1.42 ± 0.12¶	1.53 ± 0.45	1.29 ± 0.02*	0.13 ± 0.12*	0.75 ± 0.10	6.60 ± 1.63*

Note: * PH 48 hrs vs. control and PVE 48 hrs (P<0.05). ¶ PH 48 hrs vs. control (P<0.05). # PVE 48 hrs vs. control and PH 48 hrs (P<0.05).