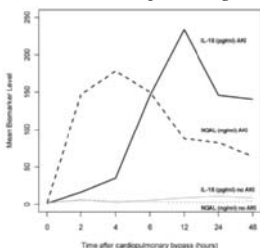


limited palliation with no long-term survivors, and irradiation in most cases is unfeasible because of local toxicity. Experience is accumulating using laser-induced thermal therapy (LITT) for treatment of recurrent, unresectable head and neck cancers leading to favorable results and apparent long-term efficacy in some cases. In this study, we review our results on 104 patients with recurrent head and neck cancer who were treated by LITT. Best results were seen in oral cavity tumors where average survival was 20.3 months (10.7–30 months; 95% CI) compared to neck (average = 14.4 months, 7.5–20.7 months; 95% CI) and other tumor sites (average = 18 months, 13.8–22.3 months; 95% CI). Tumor regrowth was not seen after treatment for an average of 47 days, with significant palliation of symptoms observed in most of these patients. Therapy response was inversely related to initial tumor volume and was dependent on both histology and growth rate. Smaller slow-growing tumors and more differentiated tumors were palliated successfully with a better local therapy response rate than poorly differentiated and rapidly dividing malignancies. The results of LITT in recurrent head and neck cancer and the prognostic factors predicting outcome in this patient population are also reviewed.

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**NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AND INTERLEUKIN-18: EARLY, SEQUENTIAL, PREDICTIVE BIOMARKERS OF ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY.** C. Parikh, J. Mishra,\* Q. Ma,\* C. Kelly,\* C. Dent,\* P. Devarajan,\* C. Edelstein,\*\* Yale University, New Haven, CT; \*Cincinnati Children's Medical Center, Cincinnati, OH; \*\*University of Colorado Health Sciences Center, Denver, CO.

**Purpose:** Acute kidney injury (AKI) is a frequent complication of cardiopulmonary bypass (CPB). The lack of early biomarkers for AKI has impaired our ability to intervene in a timely manner. In the present study, we tested whether urinary neutrophil gelatinase-associated lipocalin (NGAL) and interleukin-18 (IL-18) can be combined as predictive biomarkers for diagnosis and prognosis of AKI following CPB. **Methods:** Serial urine samples were analyzed by ELISA for IL-18 and NGAL in 20 patients who developed AKI (defined as a 50% or greater increase in serum creatinine after CPB) and 35 controls (age-, race-, and gender-matched patients who did not develop AKI after CPB). Exclusion criteria included preexisting renal insufficiency and nephrotoxin use. **Results:** Using serum creatinine, AKI was detected only 48–72 hours after CPB. In contrast, NGAL increased 25-fold within 2 hours and declined after 6 hours of CPB (Lancet, 2005). Urine IL-18 increased at 4–6 hours after CPB, peaked at over 25-fold at 12 hours, and remained markedly elevated up to 48 hours after CPB. Also, on multivariate analysis, both IL-18 and NGAL were independently associated with number of days in AKI. **Conclusions:** Our results indicate that urinary NGAL and IL-18 are increased in tandem after CPB. The combination of these biomarkers may allow for the reliable early diagnosis and prognosis of AKI at all times after CPB, much prior to the rise in serum creatinine.



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**A SINGLE-DOSE PHARMACOKINETIC STUDY OF MYFORTIC (MYCOPHENOLATE SODIUM) IN LIVER TRANSPLANT RECIPIENTS: PRELIMINARY FINDINGS.** T.W. Perry, J.F. Trotter, U. Christians, J. Bendrick-Pearl, University of Colorado Health Sciences Center, Denver, CO.

**Background:** Enteric coated mycophenolate sodium (EC-MPS) is the sodium salt formulation of the active immunosuppressive compound mycophenolic acid (MPA). This drug was recently approved for use in renal transplantation. The pharmacokinetic profile for MPS has been well studied in renal transplant recipients but has not been described in the liver transplant population. **Methods:** This study is designed to determine the pharmacokinetic profile of MPS in liver transplant recipients. Patients enrolled in this study must be  $\geq 12$  months post-transplant and on a stable dose of tacrolimus or cyclosporine for 3 months. Exclusion criteria included ALT  $\geq 235$  IU/L, serum creatinine  $\geq 2.5$  mg/dL, current use of sirolimus, mycophenolate mofetil, or azathioprine, or acute cellular rejection within 3 months of enrollment. Each patient was orally administered one dose EC-MPS 720 mg followed by measurement of blood levels of MPA at the following intervals (hours)  $t = 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 5.0, 8.0,$  and  $12.0$ . Previous renal transplant studies have defined the MPA pharmacokinetics with EC-MPS as  $t_{max}$  mean (range) = 2 h (0.8–8),  $C_{max}$  mean  $\pm$  SD =  $26.1 \pm 12.0$   $\mu\text{g/mL}$ ,  $AUC_{0-12}$  mean  $\pm$  SD =  $66.5 \pm 22.6$   $\mu\text{g}\cdot\text{hr/mL}$ . **Results:** From August to November 2005, eight patients were enrolled in this study. Demographics include 4 male/4 female, mean age = 53.4 years, mean weight = 81.2 kg. Etiology of underlying liver disease: four hepatitis C, two PBC, one hepatitis B, one hemangioma. Mean time post-transplant = 4.73 years. Results from this study showed the following pharmacokinetic parameters:  $t_{max}$  mean (range) = 2.9 h (1.5–5),  $C_{max}$  mean  $\pm$  SD =  $33.9 \pm 21.9$   $\mu\text{g/mL}$ ,  $AUC_{0-12}$  mean  $\pm$  SD =  $52.9 \pm 25.2$   $\mu\text{g}\cdot\text{hr/mL}$ .

**TABLE 1 MPA Pharmacokinetic Parameter Comparison for Renal and Liver Transplantation**

Patient Population	$t_{max}$ (h)	$C_{max}$ ( $\mu\text{g/mL}$ )	$AUC_{0-12}$ ( $\mu\text{g}\cdot\text{hr/mL}$ )
Renal transplantation recipients	2.0 (0.8–8.0)	26.1 $\pm$ 12.0	66.5 $\pm$ 22.6
Liver transplantation recipients	2.9 (1.5–5.0)	33.9 $\pm$ 21.9	52.9 $\pm$ 25.2

**Conclusion:** (1) These preliminary findings show that in liver transplant recipients, the pharmacokinetic parameters of MPA appear similar to renal transplant patients. (2) Further study is required to better understand the pharmacokinetic profile of MPA in liver transplant patients and determine if any significant differences will be noted due to underlying liver disease or coadministered immunosuppressants.

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**MAGNETIC RESONANCE SPECTROSCOPY, DIFFUSION TENSOR IMAGING, AND MAGNETIC RESONANCE PERFUSION IN THE EVALUATION OF FIBROMYALGIA PATIENTS: A PROSPECTIVE STUDY.** M. Petrou, B. Foerster, S. McLean, R. Harris, D.J. Clauw, P.C. Sundgren, University of Michigan, Ann Arbor, MI.

**Purpose:** To determine if there are significant differences between fibromyalgia (FM) patients and healthy controls using three different functional brain imaging techniques to assess for differences in a number of brain areas that have been considered to play a role in pain processing. **Materials and Methods:** All subjects (20 FM patients and 20 age-matched controls) underwent a conventional pre- and postcontrast MRI as well as completing extensive baseline clinical work-up including the McGill Pain Questionnaire and pain/pressure sensitivity testing. For 2D-CSI proton spectroscopy (TE/TR = 144/1500 ms),  $18.1 \times 1 \times 1$  cm voxels were placed in areas implicated in pain processing. Metabolite ratios were calculated for each voxel. DTI was performed using a single-shot spin-echo EPI technique along nine different directions with a b value of  $1,000 \text{ s/mm}^2$  and standardized  $50 \text{ mm}^2$  regions of interests (ROIs) were placed in a number of potential pain processing regions. For MR perfusion,  $20.50 \text{ mm}^2$  circular ROIs were placed in selected gray and white matter structures to allow calculation of relative quantitative data for mean time to enhance (MTE) and negative enhancement integral (NEI). Student's *t*-test was used for statistical analysis. **Results:** Analysis of the 2D-CSI data showed mean Cho/Cr ratios to be significantly higher in FM patients compared to normal controls in the right prefrontal subcortical white matter ( $p = .02$ ) and the left parietal white matter ( $p = .04$ ). Nonsignificant similar trends were seen in the left thalamus ( $p = .07$ ) and the left internal capsule ( $p = .09$ ). No significant differences were found in apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values between fibromyalgia patients and normal controls in most of the different regions examined. A tendency for lower FA values was found in the parietal white matter in patients with fibromyalgia compared to the normal healthy controls,  $0.256 \pm 0.026$  (mean  $\pm$  SD) vs  $0.273 \pm 0.034$ , respectively ( $p = .06$ ). Regarding MR perfusion, relative MTE values were significantly lower in FM patients compared to healthy controls in the following areas: bilateral insula, thalami, prefrontal dorsolateral gray matter, corona radiata, frontal white matter, parietal white matter, and right internal capsule. **Conclusion:** Our data suggest that there are differences between FM patients and healthy controls in brain regions that have been implicated in pain processing. Larger studies are needed to better understand the determinants and consequences of CNS changes in FM, correlate with clinical symptoms, and evaluate the potential of functional imaging in disease monitoring and therapy response.

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**PRONONCED INFLAMMATORY RESPONSE FOLLOWING CARDIOPULMONARY BYPASS ASSOCIATED WITH CENTRAL NERVOUS SYSTEM INJURY.** B. Ramlawi, J.L. Rudolph, S. Mieno, J. Feng, E.R. Marcantonio, F.W. Sellke, Cardiothoracic Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

**Introduction:** Neurocognitive decline (NCD) is a common complication in cardiac surgical patients. Its pathophysiology remains unknown, leading to significant morbidity particularly in the elderly. We studied the inflammatory response and CRP in relation to NCD following cardiopulmonary bypass and correlated this to a marker of axonal central nervous system (CNS) injury. **Methods:** Prospective cohort of 43 low-risk patients undergoing CABG and/or valve procedures using cardiopulmonary bypass were administered a neurocognitive battery preoperatively, postoperatively at day 4, and at 3 months. Battery consisted of eight validated assessments covering memory, executive function, naming, attention, fluency, and premorbid intelligence. Following published STS Consensus Statement, NCD was defined as 1 SD from baseline on  $\geq 25\%$  of tasks. CRP, interleukin (IL)-1 $\beta$ , IL-6, and IL-10 were quantified from serum with high sensitivity immunoassay and fold change (FC) calculated between preoperative/postoperative samples at 6 hours. Increase of serum tau protein after surgery (dichotomous) was used as marker of axonal CNS damage. **Results:** Cohort had an NCD rate of 45% (mean age  $72 \pm 3.6$  years). Baseline characteristics and known predictors of NCD such as age, education level, and perioperative temperature were not significantly different between patients with/without NCD. Patients with NCD had significantly higher increase of CRP, IL-1 $\beta$ , and IL-10 compared to those without NCD as described in the table below. Serum tau protein increase was significantly correlated to NCD. **Conclusions:** Increased CRP and inflammatory response perioperatively is associated with NCD in patients following cardiopulmonary bypass. Inflammation plays a key role in NCD pathophysiology, likely via axonal CNS injury, and could become a target for prevention.

Marker	NCD Group (55%)		No NCD Group (45%)		p Value	Statistical Test
	Pre vs 6 Hours-Mean	Fold diff $\pm$ SEM	Pre vs 6 Hours-Mean	Fold Diff $\pm$ SEM		
CRP	18.60 $\pm$ 5.9		4.89 $\pm$ 2.2		.019	Mann-Whitney
IL-1 $\beta$	7.14 $\pm$ 4.3		1.64 $\pm$ 0.2		.002	Mann-Whitney
IL-10	236.6 $\pm$ 102.4		30.19 $\pm$ 11.6		.01	Mann-Whitney
IL-6	5.54 $\pm$ 0.7		4.22 $\pm$ 0.6		NS	Mann-Whitney
Tau protein	78% increased		27% increased		.024	Spearman

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**APOPTOSIS GENE EXPRESSION AND ACTIVATION DURING CARDIOPULMONARY BYPASS.** B. Ramlawi, J. Feng, C. Bianchi, S. Mieno, F.W. Sellke, Division of Cardiothoracic Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

**Objective:** Cold blood cardioplegia (CBC) has been advocated as an advancement in myocardial protection during cardiopulmonary bypass (CPB) and cardioplegic arrest (CA) leading to decreased postoperative morbidity. Bcl-2, Bad, and caspase 3 are intermediates within the apoptosis cascade, which is activated following ischemia-reperfusion (IR)-induced myocardial injury. We studied the expression and modification of these apoptosis intermediates due to cardioplegia and CPB in humans within cardiac and skeletal muscle. **Methods:** Right atrial and skeletal muscle was harvested from cardiac surgical patients ( $N = 6$ ) before and after CPB, CBC, and mild hypothermia. Total and modified (cleaved/phosphorylated) caspase 3, Bcl-2, and Bad were measured by quantitative immunoblotting using specific antibodies. Microarray gene expression analysis was carried out using Affymetrix U95 GeneChip following RNA isolation. Activity of terminal caspase 3 was