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## CLOSURE OF PROTECTIVE ILEOSTOMY: COMPLICATIONS AND RISK FACTORS THAT INDICATE A BAD PROGNOSIS

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**Background:** Ileostomy closure is a common procedure done in the surgery practice, the complications and risks involving its closure tend to be underestimated.

**Methods:** 93 patients who underwent a programmed surgery of ileostomy closure.

**Results:** Complications were present in 41% of the patients: paralytic ileus 12.9%, infection of surgical wound 12.9%, rectal bleeding 5.8% pseudomembranous colitis 4.3% and death 1.07%.

The delay of time for the ileostomy closure was associated with the complications ( $p=0.041$ ) and with pseudomembranous colitis ( $p=0.003$ ). Male patients had more complications ( $p=0.042$ ) and this was associated with infection of the surgical wound ( $p=0.007$ ).

Manual End-to-end intestinal anastomosis without resection was associated with paralytic ileus ( $p=0.037$ ). There were no significant relations between complications and age, ASA, BMI, previous chemotherapy and radiotherapy.

**Conclusions:** Closure of ileostomies has a high rate of complications. This information should be taken into account when the decision of this surgery is made. The delay in waiting time from initial surgery to ileostomy closure increases the risk of complications of any kind, and also the risk for developing pseudomembranous colitis.

## COLONIC PERFORATION: PRESENTATION, TREATMENT AND OUTCOME

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**Background:** The aim of the study was to analyze presentation, treatment, and outcome of patients who were operated for colonic perforation.

**Methods:** A retrospective review of patients who underwent surgery for colonic perforation from January-2003 to December-2012 was performed. ASA score, Hinchey's classification, Mannheim peritonitis index (MPI), type of surgery, and postoperative morbidity and mortality were assessed.

**Results:** Forty-four patients (47.8%) were ASA III-IV. Sixty-eight patients (73.9%) were classified Hinchey III-IV. IPM scores  $>26$  were found in 36 patients (39.1%). After surgery, major morbidity and mortality rates were 65.2% and 34.8%, respectively. Higher mortality were found in patients  $>70$  years old ( $p=0.02$ ), high ASA grade ( $p=0.04$ ), malignancy ( $p=0.08$ ), Hinchey grade III-IV ( $p=0.015$ ), proximal perforation ( $p=0.003$ ) or IPM  $>26$  ( $p=0.004$ ).

**Conclusions:** Surgery for colonic perforation carries significant morbidity and mortality. These findings are closely related to the degree of organ reserve of patient and severity of intraabdominal sepsis.

## XENOGRAFT MODELS OF HUMAN COLON CANCER

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**Background:** The development of better animal models for human cancer is necessary to study this pathology and the application of new treatments. The aim of this study is to generate a model of colon cancer in mice.

**Methods:** Experimental groups of orthotopic colon xenografts in nude mice: I, Slices of human colon adenocarcinoma (8 mice); II, 5 million growing cells from surgical samples of colon tumor (3 mice); III, 5 million HT29 cells (10 mice). Xenografts were implanted in cecal wall. Animals were sacrificed 5 weeks later and the colon and liver were analyzed. Tumor volume was calculated in mm<sup>3</sup> using the formula X axis (minor axis)<sup>2</sup> x 0.52. Histological analysis.

**Results:** Tumor size mean (minor-maximum) mm<sup>3</sup>/metastasis: I, 48.8 (0.5-65)/ no; II, microscopic adenocarcinomas/no; III, 175.5 (14-266.2)/ hepatic metastasis in one case.

**Conclusions:** Orthotopic models of colon slices and line HT-29 can satisfactorily reproduce the human colon cancer. Further studies are necessary to obtain valid conclusions.

## THE DIFFERENTIAL PERITONEAL INFLAMMATORY MARKERS PROTEIN EXPRESSION DURING LAPAROSCOPIC AND OPEN GASTRECTOMY FOR GASTRIC CANCER. PRELIMINARY RESULTS

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**Background:** Our aim was to study the local inflammatory response depending on the surgical approach for gastric cancer assessing the protein expression of inflammation markers.

**Methods:** Prospective observational study including samples from 26 patients that underwent elective gastrectomy for gastric cancer (12 laparoscopic, 14 open). Peritoneal tissue protein expression of inflammatory response markers was studied at the beginning of the surgery and 60 minutes later employing protein array assay (Quantibody human TH17 array Raybiotech®).

**Results:** No substantial differences in the postoperative outcome were found between groups and no relevant differences were observed in the inflammatory response excepting for a diminished baseline and intraoperative expression of IL-21 in the open surgery group.

**Conclusions:** Both groups showed similar clinical outcomes and local inflammatory response patterns. However, IL-21 expression was diminished in the open surgery group, suggesting a mild impairment of the anti-tumoral cellular inflammatory response.

## HISTOLOGICAL AND BIOSCOPIC STUDY OF APPENDICULAR STUMPS TRANSECTED USING THE LIGASURE™ BIPOLAR COAGULATION DEVICE IN EX VIVO APPENDECTOMY IN HUMANS

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**Introduction:** Laparoscopic appendectomy is increasingly becoming the primary approach in the treatment of acute appendicitis. The LigaSure™ vessel sealing device has been used to transect the appendix in laboratory animals.

**Objectives:** To perform a histological and bioscopic study of the stumps after ex vivo appendectomy in humans right colectomy specimens using the LigaSure device.

**Methods:** Specimens obtained from right colectomies performed for nonappendicular pathology were studied. Conventional preparation of the samples for macro and microscopic study was performed.

**Results:** Areas of acellular material with fusion of serosal, submucosal and mucosal layers were observed. The coagulation artifact was limited. There was no communication with the caecal lumen at the sealing site.

**Conclusions:** Transection of the appendiceal stump by using bipolar coagulation (LigaSure™) in the human appendix produce the fusion of serosal, submucosal and mucosal layers. These results suggest that this technique generates optimal conditions for caecal tissue reparation and wound healing.

### EFFECTS AND OUCOME OF PREOPERATIVE BILIARY DRAINAGE ON OBSTRUCTIVE JAUNDICE PATIENTS

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**Background:** Biliary drainage can be used for palliative treatment in advanced tumors or as a “bridge” treatment to surgery, in patients with biliary obstruction due to a periampullary cancer. In this study, we analyze the usage of preoperative biliary drainage (PBD) in patients with biliary obstruction. This way, we will evaluate the effects of bile contamination and postoperative morbidity.

**Methods:** Between March 2008 and July 2013, a total of 108 patients (64 male, 44 female) were diagnosed of biliary obstruction. The pathologies were: Pancreas cancer (37%), Duodenal Cancer (4.6%), Ampullary Cancer (9.3%), Distal Cholangiocarcinoma (9.3%), Klatskin Tumor (8.3%), Gallbladder Cancer (7.4%), IPMN (4.6%), Neuroendocrine Tumor (7.4%), chronic pancreatitis (6.5%), and other pathologies (5.6%). The associated symptoms and the delay of their surgeries determined that preoperative biliary drainage was needed. In every cases biliary anastomoses was performed and samples were taken for bile culture. Complications were analyzed, pancreatic fistulas, biliary fistulas and delayed gastric emptying, among others.

**Results:** 56 patients needed PBD. The bile culture was positive in 63 cases (58.3%) and negative in 45 (41.7%). 1–5 germs were found in positive bile cultures. A total amount of 141 germs were discovered. An association within PBD and positive culture was found ( $\chi^2 = 45.86$ ,  $p < 0.001$ ). There was no association between PBD and general postoperative complications ( $\chi^2 = 1.84$ , n.s.), PBD /pancreatic fistula ( $\chi^2 = 0.707$ , n.s.), and pancreatic fistula/positive culture ( $\chi^2 = 0.002$ , n.s.).

**Conclusions:** 1. PBD is associated to positive bile cultures. 2. We have not detected association between PBD and complications. 3. When it is necessary PBD bridge therapy can be used to solve jaundice. 4. The intraoperative bile culture must be mandatory and it allows to establish a microbiological map and antibiotic resistance study in the hospital.

### KETOTIFEN REDUCES SPLANCNIC COMPLICATIONS DUE TO CHOLESTASIS EXTRAHEPATIC MICROSURGICAL MODEL IN RATS AND IMPROVES NUTRITIONAL PARAMETERS

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**Introduction:** Ketotifen, a drug that stabilizes mast cells, was administered in a cholestasis extrahepatic microsurgery experimental model to reduce hepatic-intestinal inflammatory and profibrogenesis mediators.

**Methods:** Sham-operated Wistar rats (SO), rats with microsurgery extrahepatic cholestasis (MC), half of them received ketotifen (10 mg/kg/day; oral). Body, hepatic and splenic weigh were measured. Seric hepatobiliar function parameters as well as protein and lipids levels and pro-inflammatory and anti-inflammatory mediators' levels in liver were assessed.

**Results:** Ketotifen in rats with MC decreased ascites, corporal weight, hepato-esplenomegaly, total and direct bilirubin and bile acids, with increase of the serum levels of total proteins and high density lipoproteins (HDL). It also decreased the levels of TNF- $\alpha$ , IL-1 $\beta$ , IL-17A and MCP-1 in the liver ( $p < 0.05$ ).

**Conclusions:** Ketotifen reduce hepatomegaly, splenomegaly, portal hypertension and ascites. It also could be useful in order to improve hepatic protein synthesis and reduce secondary complications due to biliary chronic liver diseases.

### REAL-TIME IDENTIFICATION OF MYOCARDIUM ISCHEMIA WITH A NOVEL FLUORESCENCE METHOD IN AN ANIMAL MODEL

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**Background:** Heart ischemia delimitation is based on preoperative imaging diagnoses. Fluorescence techniques are been developed for clinical applications. We evaluate the infarction area on a myocardium using fluorescein.

**Methods:** After IRB approval 10 NZ rabbits have been operated. Cardiac enzymes, electrocardiogram, pulse oximetry pre and postoperative were measured. After sternotomy was performed the second diagonal artery was stitched. Heart area was illuminated with Xenon and Ultraviolet light (530nm) before and after 0.01 mg / kg of fluorescein sodium 10 % (IV).

**Results:** After occlusion of coronary artery, enzyme and electrocardiogram modifications were noticed. No changes were identifying with xenon light. A dark area of  $0,7225 \pm 0.39$  cm<sup>2</sup> was captured distal to vascular occlusion after the exposure with UV (530 light). Findings were certified by pathology.

**Conclusions:** The fluorescent method was feasible and sensitive for the evaluation of a real time myocardial ischemic area.

### NEW FORM OF CHIMERISM AND ITS IMPLICATION IN CLINICAL TRANSPLANTATION

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**Background:** Transplantation of solid organs (SOT) and vascularized composite tissue allografts (VCA) requires the action of immunosuppressive drugs with the cost of their side effects. When immunosuppressive therapy is administered at lower levels, chimerism may improve allograft survival. Reverse chimerism (RC) is based on allograft repopulation by recipient cells. Our objective is to analyse clinical evidence on RC in solid organ transplantation and its relationship with allograft rejection.

**Methods:** A systematic review was performed on clinical reports of RC in SOT.

**Results:** RC in endothelial cells shows the lowest percentage in lung allografts (0.56%), while liver allografts presented the highest (46.33%). However, RC in specific parenchymal cells of SOT was present in low levels but in 73.12% of the recipients. It remains unknown if RC is the cause or the consequence of acute rejection episodes.

**Conclusions:** Clinical research should focus on allograft outcomes to be able to evaluate the effect of RC in transplantation.

### GRAFT VASCULOPATHY AND COLD ISCHEMIA IN A MODEL OF RAT HIND-LIMB TRANSPLANTATION

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**Background:** Composite tissue allotransplantation (CTA) is nowadays a clinical reality, with more than 70 transplants performed worldwide. Chronic allograft vasculopathy (CAV) is responsible of late graft loss, and has been recently observed in two clinical cases of CTA. The main histological issue of CAV is a luminal stenosis of the vascular tree due to an intimal hyperplasia and a fibrosis of the adventitia, which are responsible of the ischemia of the allograft. Different factors, either immune or not, affect the development of CAV. Cold ischemia is between the latter, as one of the factors involved in CAV in solid organ transplantation (SOT).

**Methods:** We present a rat hind-limb allotransplantation model of CAV, with the allograft exposed to a 7 hours cold ischemia at 4°C. All animals received low dose immunosuppression with cyclosporine A and were sacrificed two months postoperatively.

**Results:** We found statistically differences between the cold ischemia allotransplantation group and the group done without the cold preservation period, in both intimal proliferation and vascular permeability in large size vessels ( $p < 0.005$ ). Vascular permeability in small size vessels was also statistically different when compared in the middle and distal hind-limb thirds, between both groups ( $p < 0.005$  and  $0.05$  respectively). The same parameter diminished significantly as we progress distally in the vascular tree ( $p < 0.05$ ). A greater amount of small and medium size vessels with CAV was observed in both thirds in the cold ischemia group ( $p < 0.05$  and  $0.005$  respectively).

**Conclusions:** With this study we have demonstrated the association of cold ischemia and CAV in the experimental setting of a CTA.

#### WOUND HEALING CAN BE ENHANCED BY MESENCHYMAL STEM CELL-COATED SUTURES: INVOLVEMENT OF COLLAGEN RELEASE

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**Background:** Mesenchymal stem cells (MSCs) have demonstrated a great wound healing potential. Surgical sutures could be considered as a scaffold providing a biomechanical support to MSCs. The aim of this study was to evaluate the wound healing potential of MSCs-coated sutures.

**Methods:** *In vitro* assays of cell adhesion, phenotyping and proteomic analysis were performed using MSCs. *In vivo* assays were performed in mice and collagen deposition was quantified in sutured wounds.

**Results:** Suture pre-treatments improved the adhesive strength of MSCs to sutures. MSCs kept adhered and surrounding the pre-treated sutures, increasing the collagen content in the sutured tissue. Proteomics analysis demonstrated that collagen alpha-1(I) chain was the most abundant secreted collagen.

**Conclusions:** This is the first report showing that the implanting of MSCs via suturing may have beneficial effects on the wound healing and tissue remodeling through the release of different collagen types, constituting a useful alternative especially for patients with difficulties in healing.

#### XENOTRANSPLANTATION OF ADIPOCITIC STEM CELLS IN AN EXPERIMENTAL MODEL OF LIVER FIBROSIS BY MICROSURGICAL CHOLESTASIS

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**Background:** In humans, cirrhosis results in a high morbi-mortality rate today and an effective treatment for this severe condition does not exist. Human adipocytic stem cells xenotransplant in cholestatic-rats could improve liver fibrosis, chronic liver failure and portal hypertension.

**Methods:** 150 male Wistar rats with microsurgical extrahepatic cholestasis were either administered human adipocytic stem cells pre-differentiated to hepatocytes 2 weeks after the operation and sacrificed at 8 weeks, or saline serum.

**Results:** The rats administered the stem cells showed a decrease in ascites, porto-systemic collateral circulation, mesenteric venous vasculopathy, hepatic and spleen weight ( $p < 0.05$ ) and testicular atrophy ( $p < 0.001$ ). There was a moderate improvement in the hepatic function. A decrease in the areas of fibrosis ( $p < 0.05$ ) and biliary proliferation ( $p < 0.05$ ), with an increase ( $p < 0.01$ ) in the hepatocytes was demonstrated.

**Conclusions:** The treatment with adipose-derived stem cells could be useful for reducing complications secondary to chronic biliary liver diseases in humans. This study has been made with a Grant from FMM (Ref.nº: AP69772009).

#### ASSOCIATION BETWEEN MITOCHONDRIAL DNA HAPLOGROUPS AND THE DEVELOPMENT OF SEPSIS AND MORTALITY IN PATIENTS UNDERGOING MAJOR SURGERY

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**Background:** The influence of the genetic component on sepsis is little known. Our objective was to determine whether mitochondrial DNA (mtDNA) haplogroups are associated with an increase in the development of severe sepsis after major surgery.

**Methods:** We studied cases and controls in which mtDNA was genotyped. We studied 240 patients with sepsis and 267 patients with systemic inflammatory response syndrome (SIRS) as the control group.

**Results:** In the group of cardiac surgery patients, the haplogroup JT and the sub-haplogroup J showed an increase in the risk of developing sepsis with respect to the haplogroup HV and the sub-haplogroup H. No comparable results were observed in the group of patients that underwent abdominal surgery.

**Conclusions:** Specific mitochondrial haplogroups are associated with the development of sepsis and increase in mortality in patients that underwent cardiac surgery but not with those undergoing major abdominal surgery.

#### THE ROLE OF PROCALCITONIN AND LEUKOCYTES AS INFECTION MARKERS IN THE CARDIAC SURGERY POSTOPERATIVE PERIOD

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**Background:** The differentiation between septic and inflammatory processes in the context of cardiac surgery is often complex. Our objective was to obtain an analytic marker that would make it possible to distinguish both processes.

**Methods:** This was a prospective study that included patients that underwent cardiac surgery with extracorporeal circulation. We analysed 120 infected patients against a control group of 400.

**Results:** Mean leukocyte and procalcitonin values showed significant elevations in the group of infected patients. The variable number of times that the leukocyte value exceeded the mean value ( $13,000 \text{ cells/mm}^3$ ) during the first 3 days plus the number of times that procalcitonin values exceeded their mean value ( $1.7 \text{ ng/mL}$ ) was a parameter related to the development of infection.

**Conclusions:** Analytical evaluation using leukocytes and procalcitonin in cardiac patients can be useful in early diagnosis and monitoring of infection.

#### PERIOPERATIVE CARE PROTOCOL FOR PATIENTS ALLERGIC TO LATEX

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**Background:** Allergy to latex has actually turned out to be an important health problem.

**Objective:** Preparing a protocol for perioperative nursing cares for patients allergic to latex.

**Methods:** General action norms were defined for the perioperative circuit: Consulting Office, Hospitalization Unit, Operating Room, Postanaesthetic Recovering Unit. A list was performed with latex free articles necessary for the practice of nursing care and anaesthetic techniques as for surgical interventions.

**Results:** The protocol was applied to 15 patients and has a list with 191 latex free articles.

**Conclusions:** A perioperative nursing care protocol for patients allergic to latex offers a safe environment for the patient and therefore minimizes its risks.

#### INTRA-ABDOMINAL HYPERTENSION IN CRITICALLY BURNT PATIENTS

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**Background:** Intra-abdominal hypertension (IAH), a frequent problem in burn patients, associates higher morbimortality. We analyzed IAH prevalence, relation with mortality and surgery need.

**Methods:** prospective study 2008–2012. All critically burnt patients were included (BSA>20%). Intra-abdominal pressure (IAP) was measured with intravesical system, at admission and each 8 hours within 72 hours.

**Results:** 132 patients were admitted. Mean age 48 ± 18 years, 98% male, ABSI 8.23 ± 2.66, BSA 35 ± 22.1%. Mortality 23%. Forty-four patients (33.33%) presented IAH. Grade I (12–15mmHg) and grade II (15–20): 29 patients (21.9%), grade III (20–25) and grade IV (>25): 15 (11.3%). Complications when IAP>20mmHg were: mechanical ventilation 12 patients, shock 13, ADRS 5, kidney failure 6. Three patients needed surgery and 33.3% (grade III) and 66.6% (grade IV) died.

**Conclusions:** Up to a third of critically burnt patients presented IAH, associating increased morbidity with higher degree. Among patients with IAH, mortality was 25%, 40% when IAP>20mm Hg.

#### $\alpha_V \beta_3$ INTEGRIN-TARGETED IODINATED-RGD PEPTIDE, AS A MOLECULAR CONTRAST AGENT

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**Background:**  $\alpha_V \beta_3$ -integrins are overexpressed in solid tumors. The aim of the study was to assess the adhesion of synthetic RGD-analogues to  $\alpha_V \beta_3$ -integrins, checking their utility as a theranostic agent.

**Methods:** Fluorescence-RGD-analogues were added to cultures of CC-531 colorectal cancer cells and their fluorescence was assessed by spectrophotometry. For *in vivo* studies, 25 × 10<sup>3</sup> CC-531 cells were inoculated into the liver, and after 21 days different doses of iodine-RGD were administered through the hepatic artery or intraperitoneally. Tissue Iodine content was assessed by ICP-MS or TCMC.

**Results:** *In vitro*, after 1 h of exposure RGD are already attached to some cells, but a more intense adhesion is achieved after 2 h. Inoculation of Iodine-RGD *i.p.* rendered very low amounts of Iodine in the tumor (2.5  $\mu\text{gI}_2/\text{g-tissue}/\text{mg-I}_2$ -administered). On the other hand, when administered through the artery tumor, tissue reached Iodine concentrations 20 fold higher than normal liver tissue, and 30 times greater than via *i.p.*

**Conclusions:** RGD-analogues adhere to CC-531 cancer cells *in vitro*, and when administered through the hepatic artery selectively adhere to tumor tissue. RGD might be used as a theranostic agent.

#### PRELIMINARY RESULTS OF THE ENDOLUMINAL GASTROINTESTINAL LINER

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**Introduction:** The endoluminal gastrointestinal liner (Endobarrier) is an endoscopic and reversible device that eludes the contact between the food and the mucosa of the duodenum and proximal jejunum, simulating the effect of a Roux-en-Y gastric bypass. Preliminary studies after 1 year of follow-up show favorable effects in terms of weight loss and glycemic control of type 2 diabetic patients.

**Objectives:** We describe the effectivity and safety of the endoluminal gastrointestinal liner in patients with Class I Obesity and Type 2 Diabetes with poor glycemic control.

**Methods:** Prospective study of the first cases treated with the Endobarrier system. Variables of study: weight loss, biochemical and clinical parameters of Type 2 Diabetes prior and after 4 weeks of the delivery.

**Results:** We included 6 patients (3 men and 3 women) with an average age of 48 (range 33–60) with an initial BMI of 35.08kg/m<sup>2</sup> (range 32.60–37.12). All patients had Type 2 diabetes with a mean of 14.5 years since the diagnosis (range 1 to 29) and poor metabolic control (HbA1c 8.2%, range 5.7–12.8). 5 of the patient were treated with insulin. Delivery took nearly 30 minutes, there were no complications and patients were discharged in less than 24 hours. After 4 weeks excess weight loss was 10%. HbA1c declined to 7.5% (range 5.6–9.8) and insulin was retired in 2 out of the 5 patients. Glucose tolerance test showed a significant reduction in the AUC compared to the basal values. Compliance of the device was excellent.

**Conclusions:** Our preliminary results in terms of weight loss and diabetic control are similar to the other preclinical studies. There were no major complications and compliance of the device was excellent.

#### A NEW MODEL OF TREATMENT FOR PANCREATIC CANCER: EFFECT OF RECOMBINANT PROTEIN BMP7

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**Background:** BMP7 protein: 1) changes the morphology of fibroblasts and reduces their migration, 2) inhibits epithelial-mesenchymal transition, 3) induces mesenchymal-epithelial transition.

**Aim:** Analysis of the effect of recombinant protein human BMP7 in an experimental animal model of orthotopic xenograft human pancreatic cancer.

**Methods:** Experimental groups of the orthotopic pancreatic xenografts, 40 mice received one million Capan-1 cells: V (6 animals), vehicle-treated controls; G (11), gemcitabine 125 mg / kg / every 3 days for 21 days, B (12), BMP7 100  $\mu\text{g}/\text{kg-body-weight}/\text{day}$  for 21 days, GB (11) Gemcitabine + BMP7.

The animals were sacrificed at 21 days to assess tumor response to different treatments.

**Results:** Tumor size mean mm<sup>3</sup> (minor-maximum)/%metastasis: V, 26.3 ± 15.7 (8.5 – 38.5)/67%; G, 4.7 ± 4.2 (1.1 – 10.9)/75%; B, 14.7 ± 15.2 (0–47.4)/75%; GB, 10.9 ± 17.2 (0.1 – 41.3)/33%.

**Conclusions:** The treatment with BMP7 appears to inhibit local invasion but favor metastasis through induction of mesenchymal-epithelial transition, which is demonstrated by our results as it is the group with the largest number of metastasis.

#### INHIBITION OF MMP9 AND NUCLEAR FACTOR KAPPA B BY MELATONIN PREVENT MOTILITY AND INVASIVENESS IN HEPG2 LIVER CANCER CELLS

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**Background:** Extracellular matrix degradation by MMPs has been connected with cancer cell invasion. Melatonin, the main product of the pineal gland, exerts antiproliferative, proapoptotic, and antiangiogenic properties in human liver cancer cells. Our objective was to determine the effect of melatonin on IL-1 $\beta$ -induced migration and invasion in HepG2 cells.

**Methods:** Cell motility and invasiveness were determined by Matrigel invasion and wound-healing assays. MMP-2 and MMP-9 gelatinase activity was evaluated by zymography and their expression was analyzed by qPCR and Western Blot. MMP inhibitors expression and NF- $\kappa$ B activation were also analyzed.

**Results:** 1 mM melatonin administration reduced IL-1 $\beta$ -induced HepG2 invasion and motility through downregulation of MMP-9, while induced MMP-9-specific inhibitor, TIMP-1. Moreover, melatonin significantly suppressed IL-1 $\beta$ -induced NF- $\kappa$ B translocation and transcriptional activity.

**Conclusions:** Melatonin modulates motility and invasiveness of HepG2 cell through a molecular mechanism that involves TIMP-1 upregulation and attenuation of MMP-9 expression and activity via NF- $\kappa$ B pathway inhibition.

#### PANCREATIC TRAUMA, TREATMENT WITH PANCREATICOJEJUNOSTOMY

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**Background:** Pancreatic trauma is a surgical Challenger, due to its high morbidity. It is not a very common injury (1%) and it is normally associated to other abdominal injuries (90%).

**Methods:** Retrospective data was collected from 2007 to 2013 in patients with pancreatic traumas. Eight cases were found. Demographic and clinical data was obtained: Trauma mechanism, associated injuries, type of intervention and hospital stay. We study in depth those patients treated without pancreatic resection.

**Results:** Eight patients with pancreatic trauma were studied, with an average age 22 years old (range 15–45 years old). The most common case was blunt abdominal trauma (six patients) versus the other two patients who were injured with penetrating trauma (stab wounds). 3 of 8 patients presented only pancreatic injuries (37.5%). The rest had associated abdominal injuries: Liver (2), stomach (2), Kidney (4), Vascular (1). According to AAST classification of pancreatic injuries, there was 1 patient with grade I and Seven with grade III. Grade I was attended with drainage. Grade III was treated with. Distal pancreatectomy in 4 cases (2 with splenectomy and 2 without it). The other 3 cases were managed with pancreatoyunostomy. This cases have the same characteristics: Blunt trauma in epigastrium that produce a pancreatic fracture above de spine, they only have

pancreatic injury, clinical stability, they were evaluated in other hospital and were then send to us to receive treatment without final diagnosis, the diagnosis were done through a CT and ERCP, the operations were performed by HBP surgery team.

**Conclusions:** 1. Pancreatic trauma is still very challenging to diagnose and to treat. This type of procedure requires multidisciplinary management. It must be managed by experienced HBP surgeons for an outstanding outcome. 2. Diagnosis suspect is bases on action mechanism and clinical symptoms. 3. The CT, RM-Cholangiopancreatography and ERCP provide the exact diagnosis. 4. In selected cases with only a pancreatic trauma, a pancreatoyunostomy can be performed. Therefore, the morbidity associated to a pancreatectomy decreases.

#### PRO-COL11A1 EXPRESSION IN HUMAN PERITUMORAL FIBROBLASTS IN MODEL OF ORTHOTOPIC HUMAN PANCREATIC CARCINOMA XENOGRAFT

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**Background:** Pro-COL11A1 is a specific marker for peritumoral fibroblasts (PF). The co-injection of peritumoral fibroblasts (PF) with Capan-1 is an orthotopic xenograft model of pancreatic cancer very aggressive with great local tumor growth and the presence of metastasis. However, the animal autopsy reveals no human fibroblasts in tumors. In the present study we analyzed the address of injected PF.

**Methods:** Experimental groups (6 nude mice per group) of the orthotopic pancreatic xenografts: I, One million Capan-1 cells; II, as I+ 100.000 normal fibroblasts; III, as I+ 100.000 PF. Animals were sacrificed at four weeks after implantation to assess tumor size and the presence of metastasis. In other experiment, six mice were treated as group III, but the PF were labeled using PKH26 Red Fluorescent Cell Linker Kit system, sacrificed at 1, 2 or 3 weeks post-implantation and subsequent analysis by confocal microscopy. FISH studies and expression of pro-Col11A1 were performed.

**Results:** tumor size (mean  $\pm$  SD mm<sup>3</sup>) metastasis: I, 1.72  $\pm$  1.92; 0/5. II, 3.26  $\pm$  3.52; 1/5. III: 6.10  $\pm$  3–07; 4/5. P < 0.05. Positivity with PKH26 was observed in peritumoral area throughout the three weeks.

**Conclusions:** 1. FP stimulates the local tumor growth and metastasis. 2. We demonstrate the presence of human PF in pancreatic carcinoma orthotopic xenografts in mouse. 3. The number of PKH26 positive human FP changes over time.

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#### SPARC PEPTIDE TREATMENT IN AN ORTHOTOPIC HUMAN PANCREATIC CANCER XENOGRAFT MODEL

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**Background:** SPARC is a multifunctional protein expressed in tissues with abundant extracellular matrix. The activity of SPARC molecule has shown conflicting results in the effect on tumor progression.

**Methods:** An orthotopic xenograft model of pancreatic ductal adenocarcinoma in SCID mice to assess tumor activity: One million cells Capan-1 associated with cancer associated fibroblasts (CAFs). Three lines of treatments were applied to 40 mice: vehicle (10 mice), Gemcitabine (10 mice) and SPARC peptide F5EC (20 mice). Treatments were applied in two different periods.

**Results:** A significant weight tumor differences were found between gemcitabine group (16.0  $\pm$  17.6mg) compared with vehicle (73.1  $\pm$  21.2mg)

and SPARC ( $48.6 \pm 41.5 \text{ mg}$ ) There are not statically significant differences in number, size, macro or microscopic liver metastases respectively.

**Conclusions:** Gemcitabine continues to show greater influence as therapy when evaluating tumor weight after treatment compared to vehicle control groups and SPARC. In this xenograft model, treatment with SPARC does not seem to have a greater response than gemcitabine treated group.

#### ISCHEMIC ETIOPATHOGENY OF POST-DBE PANCREATITIS ON A PORCINE ANIMAL MODEL

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**Introduction:** The most serious complication of double-balloon enteroscopy (DBE) is pancreatitis, whose etiology has not yet been elucidated.

**Objectives:** The assessment of the relationship between the performance of a double-balloon enteroscopy (DBE) and the pancreatic perfusion modify as an etiology of post-DBE pancreatitis.

**Methods:** 20 healthy female pigs were randomly distributed into two homogeneous groups. Group I: Animals were underwent DBE for 90 minutes. Serum amylase, lipase and C-reactive protein were determined before DBE (T0), during DBE at 30 minutes (T1) and at 60 minutes (T3), at the end of DBE (T4) and 7 days of the procedure. One week after the intervention, the pancreas was removed for histological analysis and vascular endothelial growth factor (VEGF) assessment. Group II: Animals were subjected to DBE for 90 minutes and the degree of perfusion of the pancreatic left lobe was studied with two reactants: pimonidazole (Hypoxiprobe), which was administered systemically before the procedure, and Hoscht, a nuclear marker, which was injected at the moment of maximum depth insertion of enteroscope, via ultra-selective catheterization of the pancreatic branch of the splenic artery.

**Results:** No clinical signs of pancreatitis nor pancreatic enzymes alterations were detected. However, a higher decrease in pancreatic perfusion was observed by Hoscht assessment. Immunohistochemical analysis showed positive reaction to pimonidazole (hypoxia) and to VEGF (induced angiogenesis); likewise disseminated foci of ischemic necrosis were found in 47% of animals.

**Conclusions:** In this porcine model DBE hinders the vascular perfusion of the pancreas, which despite being asymptomatic, causes ischemia and necrosis foci in the organ. These results could be related to the pathogenesis of episodes of post-DBE pancreatitis in humans.

#### RELATIONSHIP BETWEEN THE LEVELS OF METALS IN BLOOD AND URINE WITH THE FINDINGS IN HAIR SAMPLES OF PATIENTS WHO HAVE UNDERGONE HIP RESURFACING ARTHROPLASTY

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**Introduction:** The elevated level of metals can provoke alterations in specific organs with unknown consequences. Hair metals monitoring could be a good indicator of this type of toxicity.

**Objectives:** To find out the relationship between the level of ion metals in serum, urine and hair in patients who have undergone metal-on-metal hip resurfacing arthroplasty.

**Method:** After several years of hip replacement surgery, the levels of metals in 45 patients in serum (Cr, Co), urine (Cr, Co) and hair (Cr, Co, Mo) were determined by ICP-MS.

**Results:** The mean levels in serum were 8.25 (Cr) and 8.38 (Co)  $\mu\text{g/L}$ , in urine 16.20(Cr) and 75.40(Co)  $\mu\text{g/L}$  and in hair 163.27(Cr)  $\mu\text{g/g}$ , 61.98 (Co)  $\mu\text{g/g}$  and 31.36 (Mo)  $\mu\text{g/g}$ . Revision surgery was needed on 11 patients. After one year, levels decreased 43.8% in chrome, 51.1% in molybdenum and 90.3% in cobalt.

**Conclusions:** There is a good correlation between the findings of metals in serum, urine and hair.

#### MICRO STRUCTURAL ANALYSIS OF METAL-ON-METAL HIP RESURFACING ARTHROPLASTY

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**Introduction:** Higher rate of follow up surgery due to failure in metal on metal devices have been reported when compared with metal-on-polyethylene arthroplasties (13% vs 3%).

**Objectives:** To know the implication of the type of alloy and the manufacturing method of the ASR™ model in clinical results.

**Methods:** The roughness (sa) analysis of the metallic cap retrieved in 11 patients. Additional analysis of the surrounding tissues under a scanning electron microscope.

**Results:** The end of the head prosthesis shows major roughness ( $S_a = 3.554$ ) than the centre ( $S_a = 1.698$ ), ( $t = -2.821$ ,  $p < 0.05$ ). Micrometric particles of wear whose composition correspond to the alloy of the prosthesis were detected near the implant.

**Conclusions:** ASR prostheses have an alloy of melted metal while the acetabular rim is treated with hot isostatic compression. All this and a high carbon content ( $> 0.15\%$ ) may explain the low resistance to wear and higher revision rate.

#### ANALYSIS OF METALLIC TRACES FROM BIODEGRADATION OF AZ31 MAGNESIUM ALLOY IN RAT ORGANS

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**Introduction:** Magnesium alloys like AZ31 present better mechanical properties and corrosion resistance than pure Mg for application as temporary implants in osteoarticular replacements. However, their biodegradation process involves the release of metallic traces (Zn, Al and Mn), in addition to Mg.

**Methods:** Cylindrical pins of AZ31 alloy 20 mm in length and 1 mm in diameter, with a weight of 28 mg (composition: 3.37 wt.% Al, 0.78 wt.% Zn, 0.22 wt.% Mn (bal. Mg)). The pins were inserted as endomedullary implants in Wistar rats to synthesise a previously induced diaphyseal femur fracture. Following euthanasia, the brain, liver, spleen, kidneys and lungs were removed, freeze-dried, and analysed by ICP-MS.

**Results:** The results show an increase in metallic traces in all the analysed organs of the animals with implants, compared to the controls, but which was only significant in the case of Al. The traces of Mg, Mn and Zn found were within the considered non-toxic limits, according to Yuen's criteria, in all the analysed organs. Only 1.39% of Al from the implant was recovered in the organs. In the brain a level of 3.11 ppm was reached (dry weight), which may be considered within the range of normal values.

**Conclusions:** Biodegradation of the AZ31 implant leads to accumulation of Mg, Mn, Al and Zn traces in the organs of the implanted rats. Only Al accumulates in a statistically significant way in the spleen. In none of the studied organs do the accumulated traces present dangerous or toxic levels.

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#### CLINICAL-RADIOLOGICAL AND HISTOLOGICAL CORRELATION OF AZ31 ALLOY USED AS A PROSTHETIC IMPLANT

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**Introduction:** The aim of this research was to assess the *in vitro* and *in vivo* biocorrosion behaviour of AZ31 Mg alloy for possible use as a prosthetic implant by Scanning Kelvin Probe and Computerised Axial Tomography (CAT). It is hoped to establish a correlation between CAT and histological findings.

**Methods:** Composition of the AZ31 alloy was: 3.37 wt.% Al, 0.78 wt.% Zn, 0.22 wt.% Mn (balance Mg). Half of the AZ31 pins were subjected to hydrofluoric acid treatment in order to improve their biocorrosion resistance. The pins were inserted as endomedullary implants in Wistar rats to synthesise a diaphyseal femur fracture. Fracture consolidation and material biodegradation were evaluated by computerised axial tomography (CAT) from the first day and after 1, 3, 5, 7, 9, 11 and 13 months. Histological analyses were carried out in parallel after 1, 9 and 13 months.

**Results:** CAT analysis showed fracture consolidation in all the animals in third and fifth months. Biocorrosion was also monitored, quantifying the formation of gas over time (cathodic biocorrosion reaction). These measurements correspond directly with the anodic biodegradation reaction of the material over time. The histological study corroborated the CAT images obtained.

**Conclusions:** The protective effect of chemical conversion treatment in HF acid found *in vitro* has not been reproduced *in vivo*. Correspondence is seen between CAT and histological analysis and both the untreated and treated AZ31 materials emerge as alternatives to the temporary materials currently in use.

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#### PLF VS TLIF IN CHRONIC LUMBAR PAIN: LONG TERM FOLLOW UP PROSPECTIVE STUDY

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**Background:** The aim of this study was to analyse physical function and pain in patients who underwent into a lumbar arthrodesis.

**Methods:** Methods Prospective randomized clinical study with a 2-year follow-up period. From March 2006 to December 2008, 66 patients were selected for either PLF (35) or TLIF (31). The patients were asked before the arthrodesis about Lumbar and root VAS and the ODI test, at the end of the follow up we reasked about these items again.

**Results:** There is statistical significant improvement in disability and pain. There were no statistically significant differences between TLIF and PLF.

	Nº MCID	Nº SCB
ODI	45 (69.2%)	33 (50%)
Lumbar VAS	44 (67.6%)	25 (37.8%)
Root VAS	37 (56.7%)	25 (37.8%)

**Conclusions:** Tlif did not improve functional outcome in patients compared to PLF. Both groups improved significantly in all categories compared to preoperatively.

#### COMPARISON OF TWO TECHNIQUES OF TENORRHAPHY. EFFECT IN THE TENSILE STRENGTH OF THE FLEXOR SINEW. STUDY IN PIG EXTREMITIES

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**Background:** The resistance of a tenorrhaphy suture is related to the number of threads that cross the zone of repair and modality of blockade of the curls.

**Objective:** To study comparatively in the laboratory by tests of traction *in vitro*, the resistance of two techniques of central suture (four ends and new model) in sinews of pig front legs.

**Methods:** 40 sinews are used, distributed in two equal groups in agreement with the type of suture. The evaluation of the tensile strength took place in a universal machine of tests with the application of constant speed. They are analyzed: separation between the ends, applied force and breakthrough point.

**Results:** Significant differences at the initial moments are not observed (separation of 2 mm). As the distance of both extremes increases, the difference becomes statistically significant ( $p < 0.05$ ) for the new suture.

**Conclusions:** Considering the mechanical resistance, the two techniques fulfill the minimum requirements but, the new technique is more efficient in terms of burst strength.

#### EVALUATION OF THE TI RELEASED IN THE SPINAL FUSION SURGERY

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**Introduction:** Instrumented spine arthrodesis is the recommended treatment for progressive spine deformity and degenerative disc disease. There is the possibility of generating microscopic metal particles that are present in the tissues of the surrounding implants.

**Objectives:** We aim to determine the serum Ti levels in patients undergoing instrumented spinal arthrodesis surgery.

**Methods:** Serum from patients (32 subjects) was collected before and after (more than 6 months) spinal arthrodesis. A double focusing-sector field ICP-MS (DF-ICP-MS) instrument was used for the total Ti determination.

**Results:** There is a statistically significant increment ( $p=0.031$ ) of the Ti concentration in the serum of the patients after surgery.

**Conclusions:** The patients undergoing instrumented spinal arthrodesis experienced a significant increase. There are not significant differences between the patients not carrying any intervertebral device and those carrying a peek® device. However, both of them show statistically different results in with respect to the patients carrying the Ti-intervertebral device ( $p=0.015$ ).

#### RELEVANCE OF LYMPHOGRAPHIC PATRON IN SURGICAL MANAGEMENT OF LYMPHEDEMA

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**Background:** The superficial lymphography made with the indocyanin green is the first step in diagnosis of lymphedema. The dermal backflows classified the lymphedema in five stages. Depending of the stage it is indicated the reconstruction with a vascularized lymphatic node flap or with the lymphovenular anastomosis. The same technique is useful to assess the clinical improve.

**Methods:** 21 patients with primary or secondary lymphedema were operated between 2011 and 2012. In every cases there were realized an indocyanin green lymphography to evaluate the lymphedemas' stage. There were classified in 5 stages. The surgical management depends on the classification. The follow up is made with the clinical exam, the measurements and another indocyanin green lymphography at 3, 6 and 12 months.

**Results:** 90% of the patients were very satisfied or satisfied with the operation. The results depend on the pre-operative stage: low staged show better results than high staged. In high grade staged the results were better with the lymphatic node flap than the lymphatico-venular anastomosis. There were no statistical differences between the clinical improve and the changes in the lymphographic stage. There were no statistical differences between measurements and the clinical changes.

**Conclusions:** The lymphedema has nowadays news possibilities of treatment. The classification of the lymphedema with the indocyanin green lymphography allows the diagnosis of lymphedema, staged it and allows the surgeon to choose between the different techniques.

**MR-LYMPHOGRAPHY: TECHNIQUE, INDICATIONS AND RESULTS**

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**Objective:** Description of the MR-lymphography technique, indications and results in the management of lower/ upper limbs lymphedema and lymphorrhea

**Methods:** From July-2012 to September-2013, MR-lymphography was performed in 20 female patients (age range 19–57 years) with primary lymphedema (2 patients), secondary lymphedema (upper/lower limbs, 16 patients) and lymphorrhea (2 patients). Studies were performed in a 3T equipment using T1-3D GRE (FLASH) sequences and intradermal injection of a gadolinium based contrast media/local anesthesia mixture in each interdigital space. Images obtained were processed into MIP and VR. Lymphatics observed were referred according to an established reference system skin marks.

**Results:** MR-lymphography allowed the study lymphatic system in all patients and to planning the lymphaticovenous anastomosis as definitive surgical treatment. In patients with lymphorrhea, injured lymphatic vessel was determined. A good intraoperative correlation was observed.

**Conclusions:** MR-Lymphography is a reliable, accurate, reproducible and save technique for the diagnosis, management and surgical planning of the lymphedema and lymphorrhea.

**STROMAL VASCULAR FRACTION- ENHANCED AUTOLOGOUS FAT TRANSFER VERSUS LIPOFILLING IN FACIAL LIPOATROPHY**

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**Introduction:** Autologous fat grafting is a promising procedure for soft tissue augmentation. However, its major limitation is fat resorption and fat necrosis that may produce unreliable results and is due to an adipose ischemic environment in the host site. In this report, we combine regenerative surgery with stromal vascular fraction (SVF) for traditional lipofilling to increase the survival of adipose tissue. The purpose of this study is to present our results using SVF mixed with fat grafting comparing the results with a control group in facial lipofilling.

**Methods:** A prospective, randomized study was conducted from 2010 to 2012. The patients and the radiologist were blinded to the allocated treatment. Ten patients with a mean age of 42.6 yrs. (20–61) affected by facial lipofilling were analyzed. Five patients were treated with SVF-enhanced autologous fat transfer and five patients underwent Coleman's lipofilling procedure. At 12-month follow-up a quantitative MRI and a photographic study were performed and patients completed a subjective evaluation with a dedicated visual analogic score.

**Results:** The mean quantity of fat injected was 22,5ml per side (hemiface). SVF-enhanced autologous fat grafting showed higher volumes compared to the control group without statistic difference. No complications were observed.

**Conclusions:** The SVF- enhanced autologous fat transfer for facial lipofilling produces an increased volume of adipose tissue at twelve months without increased morbidity.

**CLINICAL AND RADIOLOGICAL EFFECTS OF VIDEO-ASSISTED MINITHORACOTOMY FOR DIAPHRAGMATIC PPLICATION AS A TREATMENT OF DIAPHRAGMATIC EVENTRATION IN ADULTS**

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**Background:** Diaphragmatic eventration in adults can cause chronic symptoms: mainly dyspnea and orthopnea. Very few works have been published on diaphragmatic plication using thoracoscopic techniques in adults (VATS - DP). Those there are all reflect improved spirometrics, but very few have analyzed the clinical and radiological results. In our series (the second largest in casuistic with this technique), we measured these variables.

**Methods:** A retrospective longitudinal study of the patients undergoing VATS - DP over 6 years in our unit. A comparative analysis was done between the different preoperative and postoperative variables. Radiological changes were quantified using the authors' own method (Figure 1).

**Results:** All the patients (18) noticed significant postoperative symptomatic and radiological improvements, and the long-term results remained stable (Table 1). Complications were minor. There were no cases of mortality, conversions no re-operations.

**Conclusions:** VATS - DP is a safe technique that achieves significant clinical-radiological improvements in adults with diaphragmatic eventration.

**EVALUATION OF A NEW ANTIREFLUX URETERAL STENT ON PORCINE ANIMAL MODEL**

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**Objectives:** Comparison of efficacy of an ureteral stent designed to prevent vesicoureteral reflux (SARP) versus a double J ureteral stent in a porcine model.

**Methods:** 24 healthy female pigs (35–40 kg) were used. This study consisted of 3 consecutive phases. Phase I: ureteropelvic junction (UPJ) diameter of both kidneys was determined and a SARP of 3 Fr was disposed in the right upper collecting system, and a double J ureteral stent was located in the left side. Phase II: after 6 weeks, both stents were removed. Phase III: after 5 months, pathologic examination was performed in all animals. Sonographic and fluoroscopic assessments were carried out in each phase.

**Results:** UPJ diameter increase was observed between phase I versus phase II and III, however no differences were observed between both, right and left upper collecting systems. No significant differences were shown between upper collecting systems in the evolution of renal resistive index or hydronephrosis grade. Vesicoureteral reflux was found in 66.6% of animals during phase II and in a 16.6% during phase III with a double J; but no ureters with SARP had this adverse effect. Pathologic assessment did not appreciate ssd between right and left upper collecting system at level of UPJ, by contrast at the level of ureterovesical junction (UVJ) left side exhibited higher degree of injury.

**Conclusions:** The new design of antireflux ureteral stent achieves a dilation of the upper urinary tract, without affection of the UVJ, due to the device does not interfere in this area. Therefore, no adverse effects related with location of double J stent at UVJ level and bladder neck are shown with this new design. So the tolerance in patients could be presumably better than current designs.

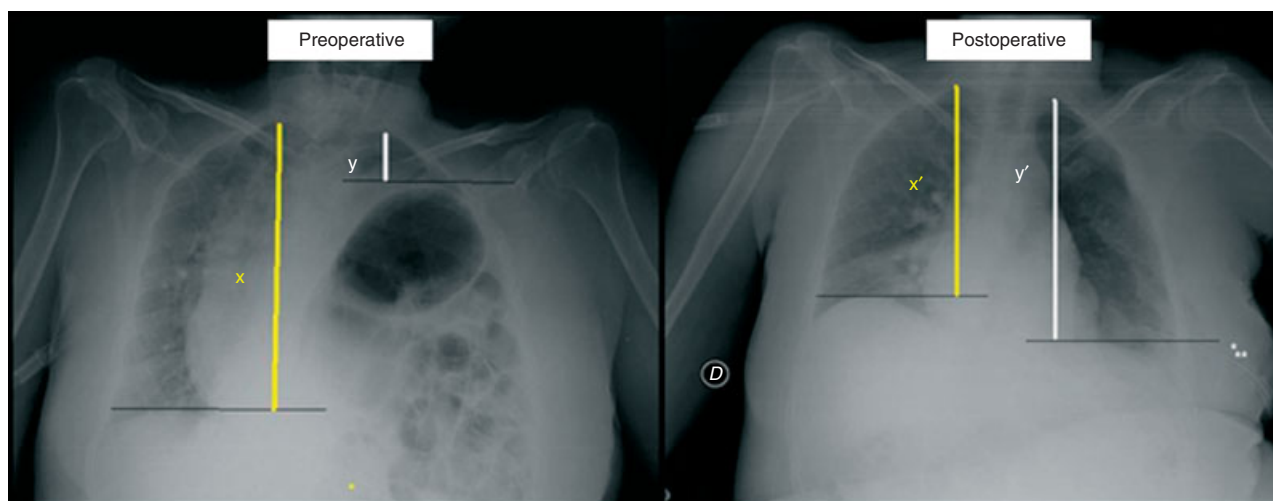
**COMPUTATIONAL MODEL OF THE UNIVENTRICULAR HEART TO AID THE SURGEON IN FONTAN PROCEDURE**

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**Background:** The aim of this work is to provide a software tool to help the surgeon getting a better understanding of the hemodynamic effects before and after the Fontan procedure.





**Fig. 1** Preoperative and postoperative radiological values. The values in centimeters of the maximum contralateral hemithorax length ( $x$  and  $x'$ ) were taken as references to quantify the changes in the operated hemithorax ( $y$  and  $y'$ )

**Table 1** Comparison of the percentage of patients who present symptoms between the preoperative stage and 3 postoperative months. Then patients at 3 months were compared with the postoperative 6, 12 and more than 30 month ones. Dyspnea = according to the “Medical Research Council” Scale, modified by the “American Thoracic Society”; Home support O<sub>2</sub> = Oxygen respiratory support at home. Figure in **boldface** (and underlined) show a percentage that is significantly different from its corresponding value for the symptom or when this value reaches 0%, so the test cannot be properly done (not underlined).

Symptom	Value	Preoperative	3 months	6 months	12 months	> 30 months
Dyspnoea	none	0%	<b><u>61.1%</u></b>	72.2%	72.2%	54.5%
	mild	5.6%	22.2%	22.2%	22.2%	45.5%
	moderate	16.7%	16.7%	5.6%	5.6%	<b>0%</b>
	serious	55.6%	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>
	Very serious	22.2%	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>
Orthopnoea	No	44.4%	<b><u>100.0%</u></b>	<b>100.0%</b>	<b>100.0%</b>	90.9%
	Yes	55.6%	<b>0%</b>	<b>0%</b>	<b>0%</b>	9.1%
Palpitation	No	<b>100.0%</b>	<b>100.0%</b>	<b>100.0%</b>	<b>100.0%</b>	<b>100.0%</b>
	Yes	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>
Dyspepsia	No	55.6%	<b><u>88.9%</u></b>	88.9%	<b>100.0%</b>	90.9%
	Yes	44.4%	<b><u>11.1%</u></b>	11.1%	<b>0%</b>	9.1%
Home support O <sub>2</sub>	No	66.7%	77.8%	88.9%	<b>100.0%</b>	90.9%
	Yes	33.3%	22.2%	11.1%	<b>0%</b>	9.1%

**Methods:** The model has been built from a physiological basis considering blood volumes in the different compartments as the model state variables. The relationships among different flows and blood pressures have been established by resistance functions of capacitance.

**Results:** The model has been proven by considering the classic Fontan procedure and the techniques from the lateral tunnel and the extracardiac conduit. The results have been validated with other authors' published data available in the literature, and with the knowledge provided by several cardiovascular surgeons with many years of experience in such interventions.

**Conclusions:** A useful tool, easy to use and low-cost, has been developed that allows the prediction of some hemodynamic variables associated to the univentricular heart.

#### CORRELATION STUDY BETWEEN MOTION ANALYSIS OF LAPAROSCOPIC INSTRUMENTS AND A SUTURING CHECKLIST

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**Purpose:** To compare assessment capabilities of a motion analysis tool against a validated checklist during laparoscopic training.

**Methods:** Construct and concurrent validation of the motion analysis tool were sought. Performance on a suturing task was rated by two experienced surgeons using a suturing checklist. Spearman's correlation between both methods was analysed.

**Results:** 18 novices, 15 intermediates and 11 experts (< 10; 11–100; > 100 laparoscopic surgeries respectively) participated in this study. Inter-examiner reliability was 0.974. There were no statistically significant differences between intermediate and expert groups regarding checklist score ( $p < 0.05$ ). Time and path length (non-dominant hand) showed statistically significant differences between the three groups. Parameters rated by the checklist related to time and

path length, showing a strong correlation with needle position. Needle position and driving also related to economy of area and economy of volume.

**Conclusions:** There is a correlation between checklist score and the tool's motion analysis metrics.

#### CHANGING THE PARADIGM: ENDOSCOPIC VIDEO ANALYSIS AND INFORMATION EXTRACTION FOR SAFER SURGERIES

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**Background:** Minimally invasive surgery creates two technological opportunities: (1) the development of better training and objective evaluation environments, and (2) the creation of image guided surgical systems.

**Methods:** Surgical video processing algorithms have been developed and validated to provide useful information about the surgical scenes and with the following goals: (1) segmentation and tracking of structures, (2) 3D reconstruction for the acquisition of the depth map of the surgical scene and (3) trocars and endoscope 3D tracking.

**Results:** Video analysis algorithms have led to the development of three environments focused on (1) cognitive skills' training (TELMA environment), (2) objective assessment (EVA tracking system) and (3) soft-tissue surgical navigation (THEMIS liver image and video navigation environment).

**Conclusions:** Video processing is presented as a solution to obtain useful surgical information allowing the localization and tracking of the elements and the 3D reconstruction of the anatomical scenario, in a non-intrusive way during the procedure.

#### INTRAOPERATIVE IMAGING IN NEUROSURGERY: INITIAL EXPERIENCE WITH CT-SCAN IN DEEP BRAIN STIMULATION AND SPINE SURGERY

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**Background:** Intraoperative imaging technologies have an ever-increasing role in surgery. The O-Arm (Medtronic intraoperative CT-scan) provides multidimensional images suitable for the neuronavigation station. The effectiveness of deep brain stimulation (DBS) and spine surgery depends on the accuracy of the location of electrodes and osteosynthesis implants.

**Methods:** A 1-year prospective compilation of patients operated on with the use of O-Arm has been performed in Cruces University Hospital.

**Results:** DBS: we have operated on 13 patients. Patient positioning adjusted to the O-arm requires a learning curve. Hypothesis previously made by microelectrode recording is confirmed in most of the cases. It also has been useful for decision-making. Spine surgery: we have operated on 74 patients and issues that affect overall surgery time are related to system positioning, operating table or surgical instruments.

**Conclusions:** We report here our early experiences with the O-arm in spine surgery and DBS. In order to overcome initial difficulties a suitable training is essential.

#### ISOLATED TRICUSPID VALVE SURGERY WITH NORMOFUNCTIONING LEFT SIDE. THE END-STAGE RHEUMATIC HEART VALVE DISEASE

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**Background:** The aim of this study was to compare early and long-term results in patients who underwent either isolated repair or replacement of the tricuspid valve with normofunctioning left side valves.

**Methods:** Forty-seven patients underwent tricuspid valve replacement (TVR) (n = 29, 61.7%) or repair (TVr) (n = 18, 38.3%). Patients undergoing TVR had the same tricuspid regurgitation (TR) degree: 3.57 versus 3.55.

**Results:** Hospital mortality was 8 patients (17.0%) and was higher among patients of the TVR group (27.6%) than in TVr group (0.0%) (p = .01). Actuarial survival curve was 30.7 ± 9.4% at 10 years and null at 20 years for TVR group. For TVr group, actuarial survival curve was 58.6 ± 12.1% at 10 years and 32.6 ± 15.3% at 20 years. Comparison between both groups shows statistical significant differences (p = 0.011).

**Conclusions:** Patients who required an isolated tricuspid valve surgery with normofunctioning left side valves have a significantly high early and long-term mortality due to cardiac and valvular causes. This bad prognosis is even worse for those patients who required a tricuspid valve replacement comparing with those who underwent a valve repair.

#### MITRAL AND TRICUSPID VALVE REPAIR WITH DURAN FLEXIBLE RING ANNULOPLASTY

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**Objectives:** We examined predictors of early and very long-term outcome after combined mitral and tricuspid valve repair with a flexible ring for rheumatic disease.

**Methods:** Between 1974 and 1999, 122 consecutive patients (mean age, 45.1 ± 12.5 years) underwent combined mitral and tricuspid valve annuloplasty with a flexible ring. Mitral repair included commissurotomy associated with a flexible annuloplasty in 98 (80.3%), and isolated flexible annuloplasty in 24 (19.7%). Tricuspid valve repair included flexible annuloplasty in 44 patients (36.1%) and annuloplasty combined with tricuspid commissurotomy in 78 patients (63.9%).

**Results:** Thirty-day mortality was 4.8%. Predictors of early mortality were previous mitral closed commissurotomy, postclamping time and reoperation for bleeding. Late mortality was 94 patients (77.1%) and the main cause was cardiac failure. Forty-six (37.7%) patients required valve reoperation, and 31 of them (67.4%) had been for progression of rheumatic valvular disease.

**Conclusions:** Combined mitral and tricuspid valve repair with a flexible ring in rheumatic disease showed satisfactory early results. Long-term results were poor because of high mortality and a high number of valve-related reoperations. The use of prosthetic ring annuloplasty was associated with a reduced incidence of both mitral and tricuspid valve reoperations.

#### EVALUATION OF POSTOPERATIVE LUNG FUNCTION AND THORACIC PAIN IN PATIENTS WITH DIFFERENT METHODS OF STERNAL CLOSURE

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**Purpose:** Comparing results of postoperative pain and ventilation parameters in patients undergoing sternal closure with nitinol clips versus patients with classic steelwire suture.

**Methods:** 140 heart surgery patients were randomized in groups performing sternal closure by steel wires suture or by nitinol clips. Both groups were comparable for sternal dehiscence risk. Spirometry and diffusion tests were performed pre and early postoperative and studied by means of pre/postoperative decremental percentages. Postoperative thoracic pain was also evaluated (absent = 0, maximum = 5).

**Results:** Deceased patients (n = 7) and prolonged mechanical ventilation and mediastinitis cases were excluded. Pain evaluation was better in nitinol group (2.5 ± 0.8) than wires group (3.7 ± 1.8). Both inspiratory and total lung capacities decrease less in group 1 than in group 0. Neither FEV1 nor diffusion test showed differences between groups.

**Conclusions:** Sternal osteosynthesis by nitinol clips decreases postoperative pain and improves respiratory function by reducing ventilatory restriction, without affecting O<sub>2</sub> diffusion nor obstructive pattern.

#### BRIDGE TO HEART TRANSPLANTATION WITH EXTRACORPOREAL MEMBRANE OXYGENATION

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**Background:** Evaluate our experience on bridge to heart transplantation (BT) in adult patients with Extracorporeal Membrane Oxygenation (ECMO).

**Methods:** In 31 patients we implanted ECMO as BT. The mean age was 54,6 years, and 20 were men.

**Results:** 30 patients were successfully bridged to transplant, with a mean supporting time of 143,2 hours. In-hospital post-transplantation survival was 76,7%, and post-transplantation survival at 12 and 44 months was 69,1% and 65%, respectively. Higher concentration of proBNP before ECMO, a venous cannula smaller 21 Fr and higher lactic acid levels during ECMO were established as independent predictors of in-hospital post-transplantation mortality.

**Conclusions:** Our outcomes post-transplantation in patients bridged only with ECMO are good enough to accept this strategy, provided that the heart transplantation is performed in the firsts 2 weeks of circulatory support and the organic function has been recovered in the meanwhile.

#### MiRNA-141: A NOVEL BIOMARKER IN PLASMA FOR RISK STRATIFICATION OF AORTIC STENOSIS

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**Background:** Calcified aortic stenosis (CAS) is a dystrophic calcification process in which osteogenic proteins play a crucial role. Several microRNAs (miRNAs) regulate this process. In particular, miRNA-141 is a repressor of BMP-2 -mediated osteogenesis. Hypothesis: Levels of miRNA-141 in plasma may be associated with valvular calcification degree.

**Methods:** We enrolled 22 patients undergoing aortic valve replacement for CAS. Total RNA was isolated from plasma and miRNA-141 was determined by quantitative PCR (qPCR).

**Results:** miRNA-141 plasmatic levels in patients with severe LVH were significantly reduced in relation to the rest of the patients ( $p=0.034$ ). There were no differences between bicuspid and tricuspid valves, therefore miRNA-141 levels are independent of valve anatomy.

**Conclusions:** miRNA-141 plasmatic levels are associated with LVH degree. We need more patients and a control group to determine connection between miRNA-141 plasmatic levels and valvular calcification and/or expression levels of osteogenic proteins. This is a preliminary study.

#### ORGANIC FUNCTION PARAMETERS UPON INTENSIVE CARE ADMISSION AFTER CARDIAC SURGERY: AN IMPROVEMENT IN ESTIMATING SURGICAL RISK?

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**Background:** The scales for staging surgical risk in cardiac surgery do not consider organic function variables. Our objective was to determine whether organic function parameters could improve risk estimation.

**Methods:** During the January 2009-January 2011 period, all the patients operated were included except for those transplanted ( $n=920$ ). We collected information on 58 preoperative, operative, ICU-admittance and postoperative variables.

**Results:** Upon ICU admittance, surviving patients compared with non-surviving ones presented differences in all the variables except for K. Univariate analysis revealed differences in lactate, MAP, bicarbonate, INR, creatinine, procalcitonin, leukocyte, heart rate and C-reactive protein. Multivariate analysis confirmed that INR, MAP, lactate and bicarbonate behaved as predictors of mortality. A risk scale was designed based on these 4 variables.

**Conclusions:** Using organic function parameters improves the estimation of surgical risk in cardiac patients in comparison with the classic scales.

#### MANAGEMENT OF GASTRIC LEAKS AND STUDY OF PREDICTORS IN THE CONTEXT OF A SLEEVE GASTRECTOMY

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**Background:** In laparoscopic sleeve gastrectomy, leaks at the staple line are important causes of morbidity and mortality. Determine the factors that may predispose to its occurrence, could ameliorate the diagnostic and therapeutic algorithm.

**Methods:** Retrospective observational study of patients subjected to GVL (207). In all cases reinforcement of stapled line was used and methylene blue test performed.

**Results:** 3.8% ( $n=8$ ) had a gastric leak (50 % of patients DM2 and 87.5% hypertension). 62.5% of patients had previous surgical history. 37.5% of leakages were detected by oral contrast, 12.5% with gastroscopy and 50% by CT. Early presentation (<48hrs) in 62.5%. Conservative management by drainage in 87.5% of patients. Two patients required reoperation.

**Conclusions:** Gastric leaks management must be based on clinical presentation and diagnostic suspicion. The presence of comorbidities or previous surgery may be an important factor to consider.

#### ROLE OF AUTOPHAGY IN INFLAMMATORY BOWEL DISEASE: A STUDY IN AN ANIMAL MODEL OF COLITIS

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**Background:** Ulcerative colitis (UC) and Crohn's disease (CD) are the two major forms of inflammatory bowel disease (IBD) and are characterized by non-specific inflammation and intestinal tissue damage. Studies have led to the identification of IBD susceptible genes, including genes implicated in autophagy, which is a process, essential for the maintenance of intestinal homeostasis.

**Methods:** Colitis was induced in Wistar rats by intracolonic administration of 30mg of TNBS. On the seventh day the rats were killed and the distal colon was collected. Analysis of LC3 and ATG16 was performed by Western blot.

**Results:** In the model of colitis increased expression of proinflammatory cytokines in agreement with macro and microscopic findings. ATG16 and LC3-II expression significantly increased in the group of rats with IBD.

**Conclusions:** Results indicate that the TNBS model show significant alterations in the autophagy process so it could be considered a model for testing new therapies.

### DNA METHYLATION BIOMARKERS FOR NON-INVASIVE DIAGNOSTIC OF COLORECTAL CANCER

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**Introduction:** The aim of the present study was to identify a panel of methylation markers useful for diagnosis of colorectal cancer (CRC) in stool DNA. Additionally, we analyze the methylation status of selected genes as a risk marker for CRC in IBD patients.

**Methods:** For the *discovery phase* we assessed DNA methylation levels using the Illumina® GoldenGate Methylation Cancer Panel I microarray (to assay 1.505 CpG sites selected from 807 genes) in 92 sporadic CRC patients. An *in silico* validation was performed for the selected probes using public datasets GSE17648 and GSE29490 (Infinium HumanMethylation27 BeadChip array). The *biological validation* of the selected methylation biomarkers was performed by pyrosequencing in three independent groups of samples: 1) 62 tumors, 32 normal-appearing adjacent mucosa and 87 stool samples were tested from 126 sporadic CRC patients. 2) 25 FFPE biopsies from surgical resections of patients with IBD-associated neoplasia. 3) colonic biopsy specimens from 39 healthy subjects. As a reference we also evaluate two previously described methylation-based marker (*Vimentin* and *Septin 9*) in a subset of these samples.

**Results:** After *discovery phase* and *in silico* validation, three genes (*AGTR1*, *WNT2* and *SLIT2*) were validated in stool DNA of affected patients with a detection sensitivity of 78% (50/64). DNA methylation of *VIM* and *SEPT9* in stool samples yield sensitivities of 55% (18/33) and 20% (7/35) respectively. In tissue 95% of sporadic carcinomas (57/60) were positive for at least one methylation marker. In IBD-associated neoplasia we found 93% of neoplastic tissues (13/14) positives. The prevalence of methylation in adjacent non-neoplastic mucosa in IBD-associated neoplasia was also higher than in mucosa from healthy controls (14/17; 82% vs 4/38; 11%;  $p < 0.001$ ).

**Conclusions:** This novel panel of specific methylation markers can be useful for diagnosis of CRC using stool DNA from CRC patients, and may help in the follow-up of high-risk IBD patients.

### PREOPERATIVE PARAMETERS FOR DIAGNOSIS OF RESIDUAL CHOLEDOCHOLITHIASIS: STUDY OF 122 PATIENTS IN THE HEALTH AREA OF LEÓN (SPAIN)

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**Background:** Acute gallstone Cholecystitis is an inflammatory (infectious) disease whose most accurate treatment is Cholecystectomy. Afterwards, Residual Cholelithiasis (RC) could be a medical complication. Therefore, the aim of the current study is to identify preoperative predictors for RC.

**Methods:** 122 patients diagnosed of acute Cholecystitis in the CAULE emergencies (September 2009 to September 2012) were retrospectively studied (54.9% male;  $60.44 \pm 17.07$  years). 108 out of 122 suffered RC. Logistic Regression was conducted having as predictors Bilirubin, SGOT, SGPT (differences between groups:  $p < 0.05$ ) adjusted by age and sex. Since ALP and GGT were only measured on 42 and 37 cases respectively, they were used as predictors in two additional logistic models.

**Results:** The RC risk is 9.4 times higher ( $CI: 1.94-46$ ) when Bilirubin is over 2.65, 15.2 times higher ( $CI: 2.5-84$ ) when SGPT is over 38, and increases with age 5 % per year ( $CI: 1.01 - 1.11$ ).

**Conclusions:** Besides Bilirubin, SGPT and age, ALP and GGT should be measured on patients with acute gallstone Cholecystitis in order to conduct a prospective study in the future.

### DRAINAGE AND MICROWAVE THERMOABLATION IN HYDATID HEPATIC CYSTS: OUR EXPERIENCE IN 3 CASES

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**Objectives:** To show the efficacy and security of combined treatment by percutaneous drainage and microwave thermoablation in non-surgical candidate patients with hydatid hepatic cyst.

**Methods:** Three patients with symptomatic hepatic hydatidosis assessed as non-surgical candidates were selected. Diagnosis was established based on ultrasound and multy-slice-CT (MSCT) findings in two of the cases and also with MRI in the third case. Cysts percutaneous drainage followed by microwave thermoablation was carried out in all patients. All the procedures were performed under previous oral mebendazol prophylaxis and under general anesthesia. Postprocedure 24h follow-up was carried out with Duplex ultrasound. MSCT was performed as 6 and 12 months follow-up imaging technique.

**Results:** Technical success was reached in 100% of the cases. MSCT follow-up showed daughter cysts disappearance, clinical improvement and also normalization of antiechinococcus serology. No post-treatment complications were reported.

**Conclusions:** The combined use of microwave thermoablation and percutaneous drainage in symptomatic hepatic hydatid cysts is an effective and secure alternative when surgery is not indicated.

### IMPACT OF DUODENAL EXCLUSION ON ENERGY EXPENDITURE AND CALORIC INTAKE IN AN EXPERIMENTAL MODEL OF OBESITY

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**Background:** We analyse changes on daily intake and expenditure energy (EE) measured by indirect calorimetry in obese and non obese animals, before and after a duodenal exclusion.

**Methods:** Male Sprague-Dawley rats non obese ( $n=15$ ) and obese by cafeteria diet ( $n=15$ ). Daily control of weight, intake, and indirect calorimetry for determine basal energy expenditure before and after surgery.

**Results:** In non obese animals, there is decrease of 20% of caloric consumption. Obese group: there is a significant decrease in caloric intake at the expense of an increase in feed intake and a decrease in consumption of cafeteria diet. A decrease in EE was observed, more significant in non-obese animals.

**Conclusions:** In non-obese animals, changes are transient. In obese animals, a significant decrease of the intake is maintained throughout the experiment. Surgical technique can influence the EE, but intake and changes of appetite are potent regulators of thermogenesis.

### KETOTIFEN REDUCES SPLANCHNIC INFLAMMATORY RESPONSE AND HISTOPATHOLOGICAL ALTERATIONS IN MICROSURGICAL EXTRAHEPATIC CHOLESTASIS IN THE RAT

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**Introduction:** Biliary fibrosis induces cholestasis. Ketotifen, a drug stabilizing mast cell membrane, reduces inflammatory response in an experimental model of cholestasis in rats.

**Methods:** Wistar rats were used: sham operated (PSO, n = 15), cholestatic (CMQ, n = 20), PSO+Ketomifen (n=15) and cholestatic rats treated with ketotifen CMQ+K (n = 20). TGF- $\beta$  serum and liver proinflammatory cytokines (TNF $\alpha$ , IL-1 $\beta$ , IL-17 and MCP-1), anti-inflammatory (IL-4, IL-10 and IL-13) and TGF- $\beta$ 1 were assessed after 8 weeks. Liver slices stained with hematoxylin eosin, Masson's trichrome and Sirius red were studied.

**Results:** IL-1 $\beta$ , IL-17 $\alpha$ , MCP-1, IL-10 and IL-13 increased in CMQ, and ketomifen reduced the rise. IL-4 and TGF- $\beta$ 1 were also increased in CMQ, but ketotifen further increased their levels. Ketotifen reduced hepatomegaly in cholestatic animals. Ketotifen reduces biliary proliferation and liver fibrosis, whereas supports hepatocyte regeneration.

**Conclusions:** Treatment with ketotifen improves gross alterations and histological findings in the microsurgical extrahepatic cholestasis in rats.

### INTRACORONARY DELIVERY OF pCSCs IN A PORCINE ANIMAL MODEL: MRI AND HISTOLOGICAL EVALUATION.

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**Background:** Despite multiple investigations carried out in the field of regenerative medicine, there are still unresolved issues. The objective of this study was to evaluate in a swine model of acute myocardial infarction the safety and efficacy of an intracoronary injection of two allogeneic porcine cardiac stem cell (pCSC) doses.

**Methods:** Intracoronary delivery of vehicle (n = 7), 25x10<sup>6</sup> (n = 7) or 50x10<sup>6</sup> of pCSCs (n = 7) was performed 1week after infarction. Troponin I (TpnI) was determined 24 hours later. Ejection fraction (EF), end diastolic (EDV) and systolic volumes (ESV) were evaluated by magnetic resonance after 10 weeks. Histological examination was done.

**Results:** No significant differences in TpnI were observed between groups. Higher EF, lower EDV, ESV values and less severe histological lesions were seen in the pCSC-treated animals.

**Conclusions:** Intracoronary administration of both cell doses appears to be safe. The pCSC-treatment seems to limit ventricular remodeling and improve cardiac function.

### EFFECT OF QUERCETIN TREATMENT ON A NONALCOHOLIC FATTY LIVER DISEASE MODEL IN MICE

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**Background:** Flavonoids appear to be capable of reducing hepatic lipid accumulation so we aimed to study the quercetin effect on NAFLD.

**Methods:** Male C57BL/6J mice fed with a methionine and choline (MCD) diet for 5 weeks were used. Quercetin was administered by oral gavage (50 mg/Kg) for this time. Histological and gene expression studies were performed in the liver and serum biochemical markers were assessed.

**Results:** MCD diet induced LXR $\alpha$  expression. Serum levels of AST and ALT were increased and serum levels of glucose and lipids were decreased in MCD-fed mice. Quercetin was able to reduce steatosis, ballooning and inflammation, as well as injury serum biochemical markers. Lower lipid accumulation was accompanied by a reduction of LXR $\alpha$  expression in MCD-fed mice treated with quercetin.

**Conclusions:** Quercetin is able to reduce NAFLD activity score so it could play an important role as an alternative therapy of NAFLD.

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### RABBIT HEMORRHAGIC DISEASE, ANIMAL MODEL OF FULMINANT HEPATITIS, INDUCES AUTOPHAGY

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**Background:** Rabbit hemorrhagic disease virus (RHDV) causes a viral hepatitis in rabbits similar to human fulminant hepatic failure (FHF); therefore it is considered a suitable FHF animal model. Autophagy is a degradative cellular process; autophagic proteins play antiviral and proviral functions. Some viruses have developed mechanisms against autophagy. Others use autophagic machinery to promote their own growth. Our objective is to study the RHDV effects on the autophagic response in this model.

**Methods:** One group of rabbits was infected with 2x10<sup>4</sup> haemagglutination units of RHDV isolate; another group received saline. Animals were sacrificed at 12, 18, 24, 30 and 36 hpi.

**Results:** LC3-II hepatic expression, specific autophagy marker, increased significantly from 24 hpi. The expression of VP60, major capsid viral protein, and LC3 was determined by immunohistochemistry showing immunoreactivity in RHDV-infected rabbits from the early infection stages.

**Conclusions:** Outcomes show that the infection with RHDV triggers an autophagic response from the early infection stages.

### EFFECT OF THE COMBINED USE OF HYALURONIC ACID, PLATELET-RICH PLASMA AND MESENCHYMAL ADIPOSE DERIVED STEM CELLS IN THE REPAIR OF THE OSTEOCHONDRAL LESIONS

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**Background:** Given the evidences that MADSC, PRP and HA can help to the repair of the osteochondral lesions, we performed a research to elucidate if the intra-articular application of a combination of these three products could improve the result.

**Methods:** 24 New Zealand rabbits. An experimental lesion was done in the condyles of the knee. A different combination of HA, PRP and mesenchymal stem cells was left in the articular cavity.

**Results:** Groups that have been treated with PRP had the best results in terms of reconstruction of the articular cartilage surface. Moreover, the PRP and HA group had the best global results. The new cartilage formed had cartilage hyaline appearance. In relation to the group where MADSC, HA and PRP were added in conjunction, the combination had not synergic effects.

**Conclusions:** Intra-articular application of a combination of PRP and HA could improve the cartilage repair by synergy.

### COMPUTATIONAL AND EXPERIMENTAL STUDY OF THE HEAT SINK EFFECT OF BLOOD FLOW INSIDE LARGE VESSELS AS A PROTECTIVE MECHANISM DURING RF-ASSISTED SURGICAL RESECTION

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**Background:** Radiofrequency (RF) assisted surgical resection minimizes intraoperative bleeding and seals vessels by creating coagulative necrosis by heating. Our aim was to assess whether the heat sink effect inside a large vessel could protect its wall during RF resection.

**Methods:** Three-dimensional models with an internally cooled electrode placed over hepatic tissue were built. We studied the effect of different factors such as device-tissue contact, vessel position and vessel-device distance (D) on temperature distributions and thermal lesion dimensions near large vessels. In vivo experiments were also conducted to validate the computational results.

**Results:** Experimental and computational lesion geometries were in agreement. Thermal lesion shape was significantly modified by the heat sink effect around the vessel, being the thermal damage to the vessel wall inversely related to D.

**Conclusions:** Experimental and computational results suggest that the heat sink effect could protect the vessel wall for  $D \geq 7$  mm.

### OPTIMIZED THORACIC BRANCH STENT-GRAFT PROCEDURE BY COMPUTATIONAL HEMODYNAMICS

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**Purpose:** Different solutions are proposed for aortic arch repair, including hybrid surgery and fenestrated implants. Surgical heaviness and hemodynamic consequences on supra aortic trunks are highly variable depending on the endovascular procedure. Some questions can be resolved by numerical modeling.

**Methods:** From pre-operative MRI, we modeled the thoracic blood flow circulation. Once calibrated the numerical model, we positioned branched stents at the innominate artery (IA) and left common carotid artery (LCCA). Each branch was simulating for antegrade or retrograde flow.

**Results:** The stent for IA passes 13.5% of antegrade flow and only 5.2% against the current. When the two prostheses are placed in the antegrade direction, infusion of 12.8% and 5.4% were obtained in the IA and the LCCA respectively, versus 4.7% and 5.7% against the current. For antegrade prosthetic IA and retrograde to the LCCA, the flow is respectively 13% and 4.7%.

**Conclusions:** If the retrograde perfusion for IA is insufficient, however the flow in LCCA prosthesis is sufficient regardless of antegrade or retrograde direction, thus facilitating the surgical procedure, decreasing the morbidity associated with cervical access. CFD is used to predict the performance of an endovascular procedure.

### AORTIC VALVE REPLACEMENT USING J-SHAPED MINI-STERNOTOMY IN PATIENTS AT MODERATE/HIGH RISK: CLINICAL IMPACT

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**Background:** Minimally-invasive approaches in surgery have made it possible to reduce inflammatory response and improve prognosis. In aortic stenosis the results observed have been dissimilar. Our objective was to evaluate the impact of minimally-invasive approaches on aortic stenosis.

**Methods:** We analysed 12 patients at moderate/high risk operated using J-shaped mini-sternotomy consecutively. These patients were then compared with a 40-patient cohort operated using the conventional approach.

**Results:** The mean EuroSCORE was 5.18. Patients undergoing minimally-invasive procedures presented shorter intensive care unit and hospital stays and fewer hours of intubation ( $p < 0.005$ ). Surgical bleeding was reduced significantly, with a lower need for blood products. A reduction in perceived pain was observed, using subjective scales.

**Conclusions:** Minimally-invasive approaches, as compared against complete sternotomy, for the treatment of aortic stenosis were accompanied by improved clinical results in a group of patients at moderate/high risk.

### THE ROLE OF PRO-INFLAMMATORY CYTOKINES IN LATE PROSTHETIC VALVE ENDOCARDITIS

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**Background:** Numerous authors have indicated the possible usefulness of humoral markers in early diagnosis and monitoring of endocarditis. Our objective was to determine if the profile of immunological expression was related to disease evolution.

**Methods:** We studied 26 patients with late prosthetic valve endocarditis, measuring interleukins IL-2, IL-4, IL-6, IL-8 and IL-10, interferon (IFN)-gamma, granulocyte-macrophage colony-stimulating factor (GM-CSF) and tumour necrosis factor (TNF)-alpha at the moment of diagnosis.

**Results:** Levels of IL-6, IL-8 and IFN- $\gamma$  were higher in the non-surviving patients ( $p < 0.05$ ). ROC curve analysis showed that IL-6, IL-8 and IFN- $\gamma$  behaved as predictors of poor development. The levels of IL-6, IL-8 and IFN- $\gamma$  were positively correlated.

**Conclusions:** The cytokines IL-6, IL-8 and IFN- $\gamma$  intervene in the unfavourable evolution of patients with late prosthetic endocarditis. Further studies are needed to confirm their potential clinical value as biomarkers.

### CHRONIC HINDLIMB ISCHEMIA: SETTING AN ANIMAL MODEL

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**Introduction:** Only 30% of patients with chronic ischemia benefit from conventional treatments, which fail in nearly 25% of them. New therapeutic tools are needed, which require adequate animal models.

**Methods:** Wag/RijCrl rats and Balb C mice were used. To mimic chronic ischemia, the femoral artery was selectively ligated under isoflurane anesthesia. Capillary flow was measured in the ischemic limb and the healthy contralateral at different study times using laser doppler (Oxford Array™).

**Results:** After ligation, capillary flow dropped to  $24\% \pm 7.1$  of basal values in adult rats, while in younger animals it only fell to  $41\% \pm 4.7$ . Two weeks later, capillary flow was partially recovered ( $41\% \pm 9.8$  and  $73\% \pm 7.3$  respectively). In mice, flow fell to  $48\% \pm 18.2$ , recovering to  $67\% \pm 29.3$  after 21 days. Immunosuppressive therapy with cyclosporine A did not change the pattern of induced ischemia.

**Conclusions:** Chronic hindlimb ischemia was successfully developed in both animal models. Adult rats show an increased susceptibility to chronic ischemia if compared to younger animals.