#### CLINICAL IMPACT OF IMPLANTABLE DEFIBRILLATORS

## HEART FAILURE IN PATIENTS CANDIDATES TO A CARDIAC SURGERY INTERVENTION: A MULTICENTRIC ITALIAN REGISTRY

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**Purpose**: clinical evidences show that the major cause of death for patients who underwent cardiac surgery intervention is heart failure.

The aim of a Multicentric Italian Registry is to evaluate the benefit of Cardiac Resynchronization Therapy (CRT) in heart failure patients candidates to cardiac surgery.

Materials and methods: in patients with LVEF < 35%, LVEDD > 55mm and QRS > 130ms or mechanical dissynchrony at TDI, an epicardial lead is positioned on the left ventricular wall and tunnellized in a subclavian pocket at the end of cardiac surgery intervention. After 3 months the patient is re-evaluated and, if the inclusion criteria for CRT remain valid, a CRT or CRT-ICD device is implanted.

In 8 Italian centers, 28 patients (18 males, age  $69 \pm 9$ ) were enrolled in the Registry. 20 patients underwent CABG procedure, the others Mitral valve repair.

Results: 18/28 patients had a 3 Month Follow-Up. Among them 7 were implanted with a CRT device and 5 with a CRT-ICD device. Two patients died after cardiac surgery intervention due to complications not related to the epicardial lead implant. No severe adverse events related to epicardial lead occurred, but in 3 patients there was a pocket edema.

**Conclusion**: Epicardial leads are safe and easy to implant, in fact no severe adverse events related to the lead occur. The Registry preliminary results show that a high percentage of patients (72,2%) need to be implanted after 3 months from cardiac surgery intervention.

## ANALYSIS OF PATTERNS OF SPONTANEOUS VENTRICULAR TACHYARRHYTHMIAS ONSET FROM IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

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Implantable Cardioverter Defibrillators (ICDs) allow storage of intracardiac electrograms (EGMs) recorded immediately before the onset of malignant ventricular tachyarrhythmias and during their course. Spontaneous ventricular tachycardia (VT) and fibrillation (VF) always originate with premature ventricular contractions (PVC). This work investigates patterns immediately preceding VT/VF onset. Data set: We considered 81 episodes from 17 patients. We investigated three possible patterns of onset: single PVC (group A: 50 EGMs, 14 patients); PVC preceded by a short-long-short (SLS) cycle (group B: 20 EGMs, 5 patients); PVC preceded by a pacing beat immediately after a previous PVC pause (PM) (group C: 11 EGMs, 3 patients). We recorded EGMs in far-field mode from St Jude Medical ICDs. Mathematical methods: We studied: (i) heart rate of VT/VF episodes (HR); (ii) spectral density, quantified by the frequency of the 50% of the signal energy (F50); (iii) correlation dimension estimated by most probable dimension value (MPDV). We used one way ANOVA to test significant differences in the mean values of the 3 groups (PVC, SLS and PM). Significant differences are accepted with P < 5% Results: Significant differences among the 3 groups are observed us-

ing F50 parameter (P = 3.1%), while HR (P > 25%) and MPDV (P >

7%) does not reach significance. It should be added that group C (PM), although does not reach significance, exhibits more frequently faster and polymorphic VT.

Conclusion: These preliminary results suggest that different modes of onset might induce different types of VT/VF.

### A NEW ALGORITHM FOR VENTRICULAR CAPTURE DETECTION IN ICDS

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Introduction: In this study a new algorithm for automatic capture verification on ICD lead systems has been evaluated. The algorithm is based on evoked response detection using the sensing vector RVcoil to Can. Combined signal amplitude and timing information for the discrimination of capture (C), fusion (F), and non-capture (NC) beats are used for classification. Method: The study was performed during new ICD implant or device replacement. Ventricular stepdown threshold testing was conducted with paced AV-delay =60ms in DDD patients or with a lower rate limit = intrinsic rate + 10bpm in VVI patients. Surface ECG and intracardiac electrograms were recorded on a wideband pacing and data acquisition system. The signals were then downloaded to a computer system, and each beat was independently classified by visual examination of the surface ECG morphology and by the algorithm. The performance was evaluated by comparison of the classification results. Results: Data from 27 patients (22 male/5 female; 64,0 ± 11,9 years) were studied, the device and lead demographics were: 18 DDD/9 VVI; 16 dedicated BP/11 integrated BP leads;19 acute/8 chronic (3,5  $\pm$  2,1 years) leads. A total of 1252 beats were analyzed: 1073 C beats, 73 F beats, and 106 NC beats. Correct detection rates for C, NC, and F beats were 95,2%, 98,1%, and 100%, respectively. Two NC beats (1,9%) in VVI mode were declared as F because of intrinsic activities. Fifty-one C beats (4,8%) were misclassified as F due to shifts in the ER signal. Conclusion: The results indicate that an accurate capture detection algorithm can be implemented using the RV coil to Can electrogram.

## CLINICAL EVALUATION OF CHANGES IN PACING THRESHOLD AND IN MORPHOLOGY OF EVOKED RESPONSE POST ICD SHO

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AUTOMATIC DETECTION OF PACING CAPTURE BY SENSING THE EVOKED RESPONSE (ER) MAY BE USEFUL FOR ENSURING NORMAL PACING FUNCTION AND INCREASE DEVICE LONGEVITY. SOFAR THIS FEATURE HAS NOT BEEN AVAILABLE IN ICD'S. THE PURPOSE OF THIS STUDY WAS TO EVALUATE THE EFFECT OF HIGH-VOLTAGE SHOCK TREATMENT ON ER SIGNAL DETECTION.

METHODS: DURING ICD SURGERY, MEASUREMENTS WERE OBTAINED ON THE PACE/SENSE PART OF THE ICD LEAD. A CUSTOM EXTERNAL PACING SYSTEM (ST. JUDE MEDICAL AB, JARFALLA, SWEDEN) PROVIDED VVIR PACING INCLUDING THE AUTOCAPTURE PACING SYSTEM AND INTRACARDIAC SIGNAL RECORDING. MEASUREMENTS WERE OBTAINED BEFORE AND AFTER DFT (DEFIBRILLATION THRESHOLD) TESTING. IN THIS ONGOING ACUTE STUDY 11 PATIENTS (59±15

YEARS, 7 MALES)WITH 8 NEW AND 3 CHRONIC LEADS FROM 2 CENTERS WERE EVALUATED SO FAR. ER SIGNAL AMPLITUDES, LEAD POLARIZATION AND PACING THRESHOLDS WERE DETERMINED.

RESULTS: MEASUREMENTS BEFORE DFT TESTING SHOWED ER AMPLITUDES (MEDIAN AND RANGE) 12.1 mV (4.9-26.5), LEAD POLARIZATIONS 0.8 mV (0.4-4.7) AND VENTRICULAR CAPTURE THRESHOLDS 0.44 V (0.25-2.0). PROPOSED ER SENSITIVITY SET-TINGS WERE 4.7 mV (2.3-11.7). AFTER SATISFACTORY DFT TEST-ING THE ER AMPLITUDES WERE 10.6 mV (3.9-33.4), LEAD PO-LARIZATIONS 0.8 mV (0.4-3.5), CAPTURE THRESHOLDS 0.5 V (0.25-1.88) AND PROPOSED ER SENSITIVITY 4.7 mV (1.2-16.6). CAPTURE THRESHOLDS WERE REPEATEDLY MEASURED AND REMAINED STABLE. ER AMPLITUDES REMAINED STABLE AND THE PROPOSED ER SENSITIVITY SETTING ONLY CHANGED IN TWO PATIENTS DUE TO CHANGING ER SIGNAL AMPLITUDE. CONCLUSION: THE INFLUENCE OF HIGH-VOLTAGE SHOCK THERAPY ON ER SIGNAL DETECTION IS MINIMAL AND THE IMPLEMENTATION OF AN AUTOMATIC THRESHOLD TRACK-ING ALGORITHM BASED ON EVOKED RESPONSE DETECTION IS FEASIBLE IN AN ICD SYSTEM.

### INCIDENCE OF CAR ACCIDENTS IN PATIENTS IMPLANTED WITH ICDS

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Patients with ICDs are normally suggested not to drive, at least in the first six months after device implant, but there is a lack of data regarding car accidents in which pts with ICDs are involved.

Our Lab performs ICD implantation since early 90es. On December 31st, 2003, 310 pts were followed-up in our outpatients clinic. In June 2004, all pts were sent a questionnaire in which they were asked to answer four question regarding their driving habits.

At the end of July 2004, 139 (98 male, mean age 62+12 yrs) patients have returned the questionnaire. 105 pts (75.5%) had a driving licence before ICD implant and only one patients was forbidden to drive after implantation for professional reasons (bus driver).

Only 7 patients out of 104 (6.7%) had a car accident, and none of them was linked to ICD discharge or tachycardia-related symptoms. Taking into consideration the incidence of accidents on the amount of patients-years of follow-up (333), the incidence is 2.1% per patients-years. Furthermore, the ICD bearers were innocent bystanders in all the event. This results are consistent with previously published data concerning pts randomized in the AVID study, in which the car accident incidence was 3.4% per patient-year, and only 0.4% per patient-year was preceded by tachycardia-related symptoms.

Our data seem to confirm that car accidents in patients with ICD are a rare event. A revision of guidelines on driving in these patients by scientific society is needed.

### PSYCHOLOGICAL EVALUATION AND INTERVENTION WITH BIOFEEDBACK IN PATIENTS WITH ICD

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Background: ICD is useful in reducing mortality, but the quality of life of patients (pts) could be deteriorated by shocks. Anxiety and depression has been described in pts with ICD. A psychological intervention could be useful in improving the well-being of these pts. Aim: We investigated the degree of psychophysical well-being in pts with ICD and monitored the effects of the device on their daily life. We also studied the utility of intervention with biofeedback (BFB) on their capacity of management of shocks.

Methods: 10 male pts (mean age 66±9, range 52-78) with ICD were studied. In the first phase we submitted our pts to psychological interviews, compilation of questionnaires (STAI X1/X2, BDI and a questionnaire on Quality of Life and Health) and the acquisition of the Psychophysiological Profile (PsP) during stress with BFB. We found three pts (mean age 55±4) with high degree of anxiety and depression (score: STAIX1=48±4; STAIX2=50±5; BDI=21±8) that we considered interventional group (IG). In the second phase the IG underwent sessions of training of relaxation with electromyograhical BFB and weekly psychological interviews. In the third phase we again submitted the questionnaires and we acquired the PsP during stress with BFB from all.

**Results**: 30% of pts with ICD had high degree of anxiety and depression and showed heavy limitations of daily activities. The pts who underwent psychological intervention with sessions of muscular relaxation with BFB have obtained a significant improvement of their capacity of management of muscular stress (p=0.05) and in the evaluation of their psychophysiological well-being (STAIX1 p=0.05; BDI p=0.05).

Conclusions: Psychological treatment is useful for getting confidence with their device and to reconsider in more adaptive terms their negative experiences.

#### CATHETER ABLATION OF ATRIAL FIBRILLATION: LONG-TERM RESULTS

### FOLLOW-UP RESULTS OF CPV RF ABLATION IN PATIENTS WITH PAF: USEFULNESS OF 7-DAYS HOLTER RECORDING.

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**Background**: Objective evaluation of paroxysmal atrial fibrillation (PAF) episodes is crucial to prove therapeutic intervention success. We juxtapose results of 24-hours and continuous 7-days Holter recordings performed in pts with PAF regarding relapses of PAF after radiofrequency catheter ablation (RF).

Methods: 45 highly symptomatic pts with drug refractory PAF underwent RF of pulmonary veins (PV), using Pappone technique (31 males, age: 55+/-8 years). Holter recordings were performed before (24 hours, H0) and after 6-9 months, (continuous 7-days recording, H7). The comparison of PAF occurrence, number and total duration was done in H0, the first day of H7 (H7F) and in H7. The patients perception of PAF was also analyzed.

Results: 6-9 months after RF 20 pts (44%) were still symptomatic (AF+) and 25 pts (56%) were without episodes of PAF (AF-). Neither asymptomatic nor non-indicated episodes were found. Patients did not differ in age, gender, heart disease and medical treatment. PAF were found in 17 pts in AF+ (85%), all indicated by patients. The comparison of H7F and next 2-7 days of H7 proved, that PAF episodes were found in 5 pts vs. 12 pts (71%) (p<0.0001). The number of episodes was 0.85+/-2.5 vs. 8.7+/-28 (p<0.005) and total duration of PAF was 5.5+/-10 vs. 16+/-25 hours (p<0.005). Maximum heart rate of PAF in AF+ pts was higher in H0 vs. H7 (152+/-4 vs. 137+/-19, p<0.05). Detection of PAF using H7 had: sensitivity-0.85, specificity-1.0, ppv- 1.0, npv- 0.89.

**Conclusions**: Holter recording is sensitive and helpful tool to assess RF efficacy in pts with PAF. Prolonged 7-days recording significantly increases sensitivity of this examination. Silent episodes of PAF were not found in this highly symptomatic population.

## RESULTS OF CATHETER ABLATION FOR CHRONIC ATRIAL FIBRILLATION USING CARTO NAVIGATED CIRCUMFERENTIAL AND COMPLEX LINEAR LESIONS

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Results of catheter ablation for chronic atrial fibrillation (CAF) using CARTO navigated circumferential lesions (CL) and complex linear lesions (LL) in the left atrium (LA) are presented. Method: Twentysix pts (7F), aged 53±11 years, underwent ablation for CAF.CAF was defined as AF lasting >3 months (mo), resistant to antiarrhythmic (AA) drugs including amiodarone (Amio), unless counterindicated, resistant to or early recurring after DC cardioversion. CAF lasted 21±28 (3-120)mo,pts took ineffectively 4.5±1.3 AA drugs,Amio was taken by 21(81%)pts.Hypertension was present in 16(62%)pts,HOCM in one, and DCM in 3pts.Mean LA diameter was 44±4.5mm, mean LV EF was 55.1±8.9%. CL with pulmonary veins (PV) isolation were combined with complex LL -connecting CL in the LA roof, connecting both lower PVs with mitral annulus (MA), connecting left superior PV along the LA appendage with anterior MA and connecting right superior PV across the septum with the foramen ovale. Results: CL never, but complex LL in majority of pts led to organization to slow monomorphic LA fltter. During the first ablation, sinus rhythm (SR) was restored during LL (septal-last in order) via LA flutter in 2pts, residual LA flutter was terminated by propafenone in 2pts and by overdrive in 1pt, DC cardioversion was required in other 21pts (failed to restore SR in 1pt). During 14.2±10 (2-33) mo F-U, 4pts had successful reablation for intermittent AF resp. LA flutter, and 2pts had unsuccessful reablation for CAF. At the end of F-U,17(65%)pts had stable SR,9 of them were free of class I or III AA drug, and only 4 of them took Amio. All pts, in whom AF terminated without need for electric cardioversion, are free of AF and Amio. Conclusion: Ablation of CAF is feasible with favorable clinical outcome. Complex LL organizing CAF into LA flutter terminable without cardioversion are associated with long-term AF free outcome.

## CATHETER ABLATION FOR PERSISTENT AND PERMANENT ATRIAL FIBRILLATION: LEFT ATRIAL ABLATION ALONE VERSUS BIATRIAL ABLATION

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**Background**: Catheter ablation of atrial fibrillation (AF) has a low efficacy in patients (pts) with persistent and permanent AF.

**Methods**: Sixty patients with persistent (35 pts) and permanent AF (25 pts) highly symptomatic and refractory to anti-arrhythmic drugs (AAD) (22 women,  $59.1 \pm 9.1$  yrs, 48 pts with structural heart disease) were prospectively randomized to 2 different ablation approaches guided by electro-anatomical mapping (CARTO). Thirty pts underwent to circumferential pulmonary vein (PV) ablation in combination with cavotricuspid isthmus ablation (approach A). In the other 30 pts the following lesions were added in the right atrium (approach B): 1) Intercaval posterior line; 2) Intercaval septal line through the fossa ovalis and the coronary sinus where a circumferential line around the ostium was performed; 3) Electrical disconnection of the superior vena cava. The clinical characteristics of the pts in the 2 groups did not differ significantly. All pts continued previously ineffective AAD at least for 6 months.

Results: During a mean follow-up of  $12 \pm 4$  months, 63% of patients (19/30) who underwent left atrial and cavo-tricuspid ablation were AF free compared with 87% of patients (26/30) who underwent biatrial ablation (p=0,039, log rank test). Post-ablation re-mapping showed the absence of discrete electrical activity inside and just around ablation lines both in the left and in the right atrium. The mean duration of procedure and fluoroscopy times for the approach A were  $165\pm26$  and  $30\pm10$  minutes, and for the approach B were  $226\pm30$  and  $40\pm13$  minutes. An hemothorax and a retroperitoneal hematoma occurred in 2 pts of the left atrial ablation group. During the follow-up left atrial flutter, which resolved spontaneously, developed in 3 pts.

**Conclusion**: This study first demonstrates that in pts with persistent and permanent AF the circumferential PV ablation in combination with linear lesions in the right atrium determines a significant higher success rate than circumferential PV ablation with cavo-tricuspid isthmus ablation alone. Our biatrial approach showed to be feasible, safe and effective to modify the right and left AF substrate. These preliminary data need to be confirmed in a randomized trial with larger population and longer follow-up.

## ADVANTAGE OF CATHETER ABLATION IN THE TREATMENT OF AF IN MITRAL VALVE PATIENTS: FOLLOW UP DURING 18 MONTHS.

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Our aim was to compare a 18 months follow up for patients with chronic atrial fibrillation (CAF) after mitral valve replacement (MVR) with/without pulmonary vein isolation (PVI) by means of radiofrequency catheter ablation (RFCA) technique.

**Method**. In 2000-2002 there were performed 63 PVI (PVI group) simultaneous with MVR for patients with CAF by means of two methods: bilateral PVI (bPVI) 26 pts and bilateral PVI with lines till mitral anulus 37 pts (modo 7). We compared the results with analogous MVR patients without RFCA (MVR group, 70 pts). CAF had been more than 6 months before MVR.

Results. During the first 48 hours sinus rhythm (SR) was obtained for 61 pts in PVI group (97%) and for 51 pts in MVR group (73%), on the 7th day in PVI group for 59 pts, in MVR group for 44 pts. With stable SR were discharged 55 pts in PVI group (87.3%) and 41 MVR pts (58.5%). After 3 months SR with AAD in PVI group was observed for 49 pts (78%), besides, 81.8% (30 pts) of them were in MVR modo 7 group; During follow up stable SR with AAD in PVI group in 18 months remained for 47 pts (75%), in modo 7 group 30 pts (81%), bPVI group 17 pts (65%). In MVR group SR remained for 11 pts. (15%), the rest regained CAF 45 pts (64%). The difference in the effectiveness of SR maintenance was significant (p<0.001) in PVI and MVR groups (75% vs 16%).

Conclusions. PVI with RFCA is a safe and effective method for SR maintenance in valve surgery patients when compared with conventional replacement. Linear ablation for SR maintenance is more efficient as PVI. AAD in postoperative period must be used permanently and are more efficient for patients after RFCA.

### COMPARISON BETWEEN INTEGRATED AND ANATOMICAL APPROACH FOR PULMONARY VEINS ABLATION

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Pulmonary vein (PV) disconnection by catheter radiofrequency (RF) ablation has been reported to cure atrial fibrillation (AF). Different techniques have been proposed. Aim of this study was to compare the outcome of a pure anatomical with an integrated approach (anatomical and electrophysiological).

Methods. Sixty consecutive patients (pts) affected by drug refractory AF, were assigned to two different approaches. Group A consisted in 30 pts (mean age 55±7 years) affected by paroxysmal (18), persistent (8) and permanent (4) AF that underwent PVs ablation by means of a pure anatomical approach. Group B consisted of 30 consecutive pts (mean age 52 ± 9 years) affected by paroxysmal (21), persistent (5) and permanent (4) AF that underwent RF ablation of PVs by means of an integrated approach. In all pts RF ablation was performed with Carto system in order to create circumferential lines around each PV. In Group B pts the persistence of PV potentials was then assessed. If PV potentials persisted, RF pulses were delivered targeting the electrophysiological breakthroughs to disconnect PVs.

Results. Total procedure duration, fluoroscopy time, and RF delivery time were:  $227\pm43$ ,  $55\pm23$  and  $43\pm16$  minutes (group A),  $232\pm32$ ,  $51\pm15$  and  $42\pm10$  minutes (Group B) respectively (ns). After  $15.4\pm7.4$  months, 17 pts (57%) of group A and 25 pts (83%) of group B were in stable sinus rhythm (p<0.05). Of group A 13 (76%) sinus rhythm pts were on anti arrhythmic drugs, while of Group B 15 (60%) sinus rhythm pts discontinued all drugs after 6 months (p<0.05). Four pts (13%) of both Groups underwent two procedures.

Conclusions. PVs ablation by means of an anatomical and electrophysiological integrated approach seems more effective than a pure anatomical RF ablation approach. Electrophysiological confirmation of PVs disconnection could be an useful successful marker of RF treatment of AF

#### INTRAOPERATIVE ABLATION OF ATRIAL FIBRILLATION

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**OBJECTIVE**. Surgical treatment of atrial fibrillation requires specific atrial partitioning (Maze operation). Replacing surgical incisions by means of various sources of energy allows a rapid and reliable procedure

**METHODS**. From January 1998 to September 2003, 91 patients with chronic atrial fibrillation (average duration 34 month)underwent a modified Maze operation by means of microwaves, radiofrequency or ultrasound.

Patients in group A (84Pts) had mitral valve disease (61 Pts) or both mitral and aortic (23Pts) or atrial septal defect (2Pts).

Patients in group B (9Pts) had IHD (7Pts) or aortic valve disease alone (2Pts).

Procedure was performed by means of microwaves in 46 cases (all the cases in epicardial approach), radiofrequency in 38, ultrasounds in 7. Amputation of left atrial appendage and cryoablation on mitral and tricuspid valve annuli were added when in all cases.

**RESULTS**. Early mortality rate was 3.2%. Seven patients required prolonged inotrophic support.

There was recovery of synus rhythm in 68 patients in the immediate postoperative period. Five Pts in Group A needed PMK implantation (5.4%) The followup showed synus rhythm in 53 patients in Group A (63%) and 5 Pts in Group B 71%).

**CONCLUSIONS.** Various sources of energy can be used intraoperatively for a safe treatment of chronic atrial fibrillation in a significant percentage of Pts. Our current investigations are directed towards the optimal source of energy and approach required for a fast and safer procedure.

## COMBINED ABLATION STRATEGY (ANATOMICAL AND ELECTROPHYSIOLOGICAL) FOR PERSISTENT ATRIAL FIBRILLATION.

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The aim of this study was to evaluate the results of an ablation strategy based on a combined anatomical and electrophysiological approach in patients (pts) with persistent atrial fibrillation (AF).

Methods: 16 pts, mean age 56 +/- 6 years, 12 Males, with recurrent persistent drug refractory AF (pre-ablation AF duration 12+/-3 months) underwent left atrial catheter ablation. The left atrium diameter was 4.2+/-0.3 cm. The left ventricular ejection fraction was 59+/-3.8%. RF lesions were delivered through an irrigated-tip 3.5 mm ablation catheter (Navi-Star Thermo-Cool, Biosense Webster) to obtain a complete encircling of right and left pulmonary veins, about 1 cm proxymal to the veins ostium, guided by the CARTO system (Biosense Webster). A linear lesion from the left inferior pulmonary vein to the mitral annulus was also performed and it was not electrophysiologically validated. This anatomical approach was integrated with an electrophysiological endpoint: all the pulmonary veins potentials around a decapolar LASSO positioned at each pulmonary vein ostium had to be eliminated at the completion of the encircling lesions. If this was not the case, further LASSO guided RF applications were delivered more ostially up to the complete pulmonary vein disconnection.

Results: all the procedures were completed without any major or minor complication. During a follow-up of 15.9+/-11.3 months, 15/16 pts (93%) were in stable sinus rhythm. Ten pts were free from AF recurrence (4 on antiarrhythmic drugs) after the first procedure

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(62.5%), and additional 5 pts (31%) required a second ablation performed within 60 days. One pt didn't benefit from ablation. Conclusions: a combined ablation strategy using both an electrophysiological (LASSO demonstration of pulmonary veins disconnection) and anatomical (CARTO guided) approach is an effective treatment for persistent AF in pts with normal left ventricular function and slightly dilated left atrium.

## MULTI-DETECTOR COMPUTED TOMOGRAPHY WITH DEDICATED PULMONARY VEIN RECONSTRUCTION SOFTWARE PRIOR TO PULMONARY VEIN ISOLATION

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Aim: Pulmonary vein (PV) isolation for atrial fibrillation represents an increasingly useful but technically challenging treatment technique for the electrophysiologist. The procedure may be facilitated by prior detailed demonstration of the left atrial (LA) and PV anatomy and it is possible that the use of multi-detector computed tomography (CT) for this purpose may reduce procedure times and complication rates. Novel CT reconstruction software is now available specifically for eletrophysiology cases. Our aim is to demonstrate the type of CT reconstructions possible and to show the variations in anatomy that we have encountered.

**Methods**: Multi-detector CT (GE Lightspeed 16, GE Medical Systems) scans are acquired using retrospective ECG gating. A sub-millimetre collimation (16 x 0.63 mm) is used and a partial segmental reconstruction algorithms to provide a temporal resolution of 125 mseconds. The LA and PVs are evaluated using dedicated software (CardEP, ADW 4.2 workstation, GE Medical Systems) to reconstruct multiplanar reformats and semi-automated 3D volume rendered images both of the surface and 'within chamber' anatomy.

**Results**: To date LA and PV reconstructions, using the dedicated CardEP software, have been completed for 18 patients. Wide variation has been shown in the LA appendage anatomy and in the PV drainage. One patient, with a previous secundum atrial septal defect repair, was found to have an inferior sinus venosus defect. Examples of normal and unusual anatomy will be shown.

Conclusion: State of the art multi-detector CT software enables the imaging cardiologist to reconstruct LA and PV images of a type that were previously not available. There is variation in the anatomy of patients undergoing PV isolation procedures and this may now be elegantly demonstrated. We would advocate that multi-detector CT should precede pulmonary vein isolation procedures and that dedicated software should be available for image analysis.

#### ATRIAL FIBRILLATION ELECTRICAL PREVENTION AND TREATMENT

#### EVALUATION OF DYNAMIC ATRIAL OVERDRIVE STIMULATION EFFECTS IN STRUCTURAL REMODELING OF ATRIUM IN PATIENTS WITH CHRONIC ATRIAL FIBRILL ATION.

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**Introduction**: The structural remodeling, involved in the AF physiopathology, it is characterized by increase of the mass, distention and atrial fibrosis, reducing the transport speed and perpetuating the multiples circuits of having reentered.

**Objective**: to evaluate the cardiovascular effects under the algorithm DDD+ treatment (dynamic overdrive stimulation).

**Methods**: The study was prospective, randomized, controlled, double-blind, crossed-over, that has included patients with recurrent chronic AF associated with bradycardia. Patients were randomized in 2 groups in agreement with the stimulation mode: DDD and DDD+. The first evaluation was accomplished after one month implant, the second in 6 months and the third after the crossover, in 12 months. To each evaluation a Doppler echocardiography was accomplished, according to international standards. (Alpha=5%, IC 95%)

**Results**: they were appraised 34 patient, 54% female, average age of 61,4 $\pm$ 13. To the analysis of the echocardiogram, there was gets better significant in the diameter diastolic end of the right ventricle in the group DDD+ when compared to the group DDD (p < 0,05). In the same way, significant reduction was observed in the left atrium diameter in these patient ones (p < 0,01), varying of 46,8 $\pm$ 6,1 mm before the implant to 38,4 $\pm$ 4,7 at the end of the study with DDD+. There were not differences us other indexes of the echocardiography. **Conclusions**: The overdrive atrial algorithm improved the ventricular diastolic function, reducing significantly the left atrium diameter and suggesting its action in the structural atrial reverse remodeling.

### PACE PREVENTION OF ATRIAL FIBRILLATION: RESULTS FROM THE VIP REGISTRY

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Pacemaker (PM) therapy is one of the interventional techniques to prevent recurrent atrial fibrillation (AF). So far, preventive pacing did demonstrate only a moderate and clinically not convincing effect in non-selected patients with recurrent AF. Therefore, the VIP (Vorhofflimmer(AF)-prevention by Individualized pacemaker Programming)-registry was initiated to identify subgroups of patients being more likely responders to preventive pacing algorithms.

**Methods**: The registry includes 624 pts. with recurrent AF and conventional indication for PM. Patients received a dual chamber device with detailed AF diagnostics and 4 different preventive algorithms (Selection series, Vitatron). Following implantation a 3 month diagnostic phase with conventional pacing identified pts. with substrate-AF (>70% of AF episodes with <2 premature atrial contractions (PACs) before AF onset) from trigger-AF (<70% of AF episodes with <2 PACs before AF onset). For a consecutive follow-up of 3 month pts. with trigger-AF were programmed to PAC-initiated preventive pacing algorithms whereas pts. with substrate-AF underwent continuous overdrive pacing.

**Results**: 161 patients completed so far diagnostic and preventive pacing phases: Comparing the AF subgroups, pts. with trigger-AF and AF burden of >1% exhibited an AF burden reduction of 32.6% (Mean AF burden: 9.7% vs 6.5% with preventive pacing, n.s.) whereas pts. with substrate-AF demonstrated an increase in the mean AF

burden of 14.9% while performing preventive pacing (Mean AF burden: 10.6%/diagnostic phase vs 12.5%/preventive pacing).

Conclusions: Patients with trigger-AF demonstrate a relative reduction of 32.6% in AF burden with preventive pacing compared to patients with substrate-AF who demonstrated an increase in AF burden while performing continuous atrial overdrive pacing. The results of this pacemaker registry indicate that patients with trigger-AF are more likely responders to preventive pacing.

### LONG-TERM CLINICAL EFFECT OF PREVENTIVE ATRIAL PACING ALGORITHMS IN PAROXYSMAL ATRIAL FIBRILLATION

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Several studies have shown poor efficacy of atrial pacing algorithms implemented in designed pace-makers (PM) for prevention of paroxysmal atrial fibrillation (AF). However, in most of these studies AF burden and time to first AF recurrence after PM implantation were used for evaluation of effectiveness of these algorithms. Aim of our study was to investigate long-term effect of atrial pacing algorithms of Medtronic AT 500 PM, by using clinical parameters as persistence of sinus rhythm (SR), number of hospitalizations and of external cardioversions related to AF episodes and use of warfarin before and after PM implant. To this purpose, 74 pts (mean age 68±12 years) with sick sinus syndrome (SSS) and persistent or paroxysmal AF (at least 2 episodes\month of >24 hours duration AF in the two months preceding PM) were implanted. After pacing, anti-arrhythmic therapy remained unchanged in all pts.

Results: after a mean follow-up of 36±7 months, 60 pts (81%) showed predominant SR, although with few, short-lasting (max 4 hours duration), self-terminating AF episodes. Prevention algorithms of the PM, providing continuous overdrive atrial pacing, led to a significant decrease of number of hospitalizations (138 vs 24) and of external cardioversions (77 vs 13) related to AF recurrences; moreover, after PM implant the number of pts treated with warfarin (shift to aspirin) decreased over time (68 vs 24 at the end of follow-up).

**Conclusions**: in pts with SSS and frequent AF episodes, prevention algorithms of Medtronic AT 500 PM appeared highly effective in long-term maintaining of sinus rhythm; moreover, they reduced the need of warfarin use and provided a marked reduction of hospitalizations and of external cardioversions due to AF recurrences.

### EFFECT OF AT500 ON HOSPITALIZATION, CARDIOVERSIONS, SYMPTOMS AND MEDICATION

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The AT500 device provides enhanced monitoring and therapies for atrial (A) tachyarrhythmias. This study analyses the effect of AT500 therapy on patient (pt) hospitalization, cardioversions, symptoms and use of antiarrhythmics (AA) and anticoagulation.

METHODS: 384 patients (53% male, age 69±11years) with intermittent atrial fibrillation (AF) / atrial tachycardia (AT) were followed for 31.5±27.5 weeks. Data was collected at enrollment (enr) and during follow-up (fu):

**RESULTS:** After one year of fu, a significantly higher number of pt has been diagnosed to have AT (60%). The number of pt treated with coumarin, aspirin, and AA also significantly increased (67%, 65%, 60%-300% respectively). The number of pt with cardioversions, hospitalizations, any symptoms, dizziness and syncope was significantly lower (50%, 25%, 15%, 38%, 75% respectively) after 1 year of fu, as was the mean number of cardioversions per pt.

**CONCLUSION**: The higher incidence of A arrhythmias after implantation of AT500 is probably the result of better pt monitoring. It seems that better pt monitoring led to more aggressive medical treatment with anticoagulation and AA, and resulted in fewer cardioversions with fewer pt requiring hospitalization.

	% pt at enr (mean ±sd)	Difference to fu at 12 month (mean ±sd)	р
Hospitalization	57.1±2.7	-14.0±4.6	0.002
Cardioversions	36.2±2.5	-17.1±3.7	< 0.001
Dizziness	45.1±2.5	-17.3±4.2	< 0.001
Syncope	20.3±2.1	-16.1±2.5	< 0.001
Any symptoms	86.2±1.8	-12.8±3.61	< 0.001
Primary A contraction	29.1±2.3	+9.3±4.3	0.031
A tachycardia	25.0±2.27	+15.8±4.0	< 0.001
A flutter paroxismal	34.8±2.4	+13.4±4.2	0.001
A flutter persistent	4.7±1.1	+4.9±2.4	0.040
AF persistent	10.4±1.6	+6.6±3.1	0.032
AF permanent	1.0±0.5	+4.2±1.7	0.016
Coumarin	36.5±2.5	+24.1±4.0	< 0.001
Aspirin	29.2±2.3	+18.8±4.2	< 0.001
AA class I	9.6±1.5	+9.5±3.1	0.002
AA class II	25.5±2.2	+16.5±4.0	< 0.001
Amiodarone	23.4±2.2	+13.5±3.9	< 0.001
Sotalol	16.4±1.9	+10.9±3.5	0.002
AA class IV	3.9±1.0	+9.8±2.5	<0.001

### TOLERABILITY OF PACING ALGORITHMS FOR ATRIAL FIBRILLATION (AF) PREVENTION

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Pacing algorithms designed to prevent AF may induce atrial overdrive and consequently a higher heart rate that could be not tolerated by the patient (Pt). Aim of the study: The SEPT (Side Effects of Pacing Therapies) is a prospective, randomized, cross-over study to evaluate the tolerability of specific algorithms for AF prevention, with respect to conventional DDD(R) stimulation. Methods: 32 Pts with SSS brady-tachy were enrolled and implanted with Vitatron Prevent AF or Selection 9000 pacemaker (pm) equipped with specific AF algorithms and Holter functions. Two weeks after implant Pts were randomised: DDD(R); DDD(R)+Pace Conditioning (PC) to continuously overdrive the atrium, DDD(R)+ premature atrial contraction related algorithms (Alg), 1 month each. The maximum pacing rate related to AF prevention algorithms was limited to 100 bpm by programmation. Rate responsive function was activated according to brady indication for pacing and kept constant for the whole study period. At follow-up Pts were evaluated during exercise and through the Specific Symptom Scale referring to the previous month. Symptoms due to arrhythmias were excluded by comparing the diary of the Pt with data stored by the pm. Results: 24 Pts were symptoms free at each randomisation phase and during exercise. Soon after programmation 2 Pt requested an early cross-over, when atrial overdrive was programmed ON, without AF episodes. Six Pts did not perform the exercise stress test due to non cardiac reasons. The mean pacing % was 64% in DDD(R), 95% in DDD(R)+PC, 81% in DDD(R)+Alg. Conclusions: all pacing algorithms are well tolerated by Pts both during exercise and in normal life, excepted continuous atrial overdrive in 2 cases.

### THE EFFECT OF PACING ALGORITHM FOR SUPPRESSION OF ATRIAL FIBRILLATION

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Background: Various pacing algorithm (PA) according to onset mechanism (OM) of atrial fibrillation (AF) have been developed. However, how to select these PAs and those effect on AF have not been investigated in detail. The purpose of this study was to determine the effect of PA on AF. Methods: This study consists of 8patients (3males, mean age 69.2\_}5.6years) who received Vitatron's Selection pacemaker (PM) with at least 1 AF detection during 3months after implantation. PA was turned off and on for 3months by crossover method. Each PA was assigned according to OM of AF in each patient, i.e., Pace Conditioning for sudden onset (SO) and multiple PAC (MPAC), PAC Suppression for MPAC and short run (SR), Post PAC Response for short-long sequence (SL), and Post Exercise Response for sudden rate drop prior to AF. We compared atrial pacing dependency (%pacing), number of AF episodes, cumulative AF duration, number of PAC, and OM of AF stored in PM between each setting. Result: %pacing was greater during PA turned on than turned off (84.5\_}22.9% vs 55.6\_}34.7%). Number of AF (100\_}167.3 vs 142.6\_}250.2), cumulative AF duration (4071.9\_}9898.4min vs 7866.8 \12846.8min) and number of PAC (37756.9 \34683 vs 77658.1\_}146754.7) decreased during PA turned on though these differences were not statistically significant. PM stored 60OMs (SO 50%, MPAC 25%, SR 23.3%, SL 1.7%) during PA turned off and 41OMs (SO 48.8%, MPAC 34.1%, SR 17.1%) during turned on. Conclusions: PA failed to decrease AF significantly. This might be associated with insufficient patient population and follow-up duration. Furthermore, OM sometimes changed after PA turned on. Therefore, the effect on AF during all PAs turned on must be investigated.

## RANDOMIZED COMPARISON BETWEEN ATRIAL ATP THERAPY SETTINGS: SECONDARY ENDPOINT OF THE PITAGORA TRIAL

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BACKGROUND. IN PATIENTS SUFFERING FROM BRADY-TACHY FORM OF SINUS NODE DISEASE(BT-SND) VERY OFTEN ATRIAL FIBRILLATION AND MORE REGULAR ATRIAL TACHYARRHYTHMIAS(AT) COEXIST. AIM OF THE PITAGORA PROSPECTIVE, RANDOMIZED, MULTICENTRE STUDY WAS TO EVALUATE THE IMPACT OF PHARMACOLOGICAL AGENTS AND ANTITACHYCARDIA PACING THERAPIES(ATP) IN THE TREATMENT OF AT EPISODES IN BT-SND PACED PATIENTS.

METHODS. WE ENROLLED 163 PATIENTS(65 M, MEAN AGE 71±9), IMPLANTED WITH A DUAL CHAMBER DDDRP

#### ATRIAL FIBRILLATION ELECTRICAL PREVENTION AND TREATMENT

PACEMAKER(MEDTRONIC AT500O). AT IMPLANT, PHARMACOLOGICAL THERAPY WAS RANDOMIZED BETWEEN IC CLASS AND III CLASS AGENTS. AFTER AN OBSERVATIONAL PERIOD OF 5 MONTHS AFTER IMPLANT, ATP THERAPIES WERE ENABLED, SELECTING RAMP OR BURST+ IN A RANDOMIZED WAY, MAINTAINED FOR 4 MONTHS AND THEN CROSSED OVER.

RESULTS. IN A MEAN FOLLOW UP OF 13 MONTHS, 81 PATIENTS SUFFERED 3816 AT EPISODES, WITH A MEDIAN NUMBER OF 35 EPISODES PER PATIENT. IN 44 PATIENTS, 893 AT EPISODES WERE TREATED AND 492 (55.1%) TERMINATED. BURST+ TERMINATED 187 OUT OF 375 AT EPISODES (49.9%) IN 32 PATIENTS. RAMP TERMINATED 305 OUT OF 518 AT EPISODES (58.9%) IN 34 PATIENTS (P=0.008 VS BURST+). 22 PATIENTS SUFFERED AT EPISODES IN BOTH CROSS OVER PERIODS AND ALLOWED A PAIRED COMPARISON OF ATP THERAPIES EFFICACY: 124 EPISODES OUT OF 236 (52.5%) WERE TERMINATED BY BURST+, WHILE 230 EPISODES OUT OF 359 (64.1%) WERE TERMINATED BY RAMP (P<0.005 VS BURST+). IN 13 PATIENTS WHO HAD AT LEAST 6 EPISODES TREATED BY BOTH THERAPIES, MEAN ATP EFFICACY PER PATIENT WAS 45.1 FOR BURST+ AND 59.2% FOR RAMP (P=0.29).

**CONCLUSIONS.** THESE PRELIMINARY RESULTS SHOW THAT, IN BT-SND PATIENTS ENROLLED IN PITAGORA TRIAL, ATP THERAPIES WERE ABLE TO TERMINATE APPROXIMATELY HALF OF TREATED EPISODES. IN PARTICULAR RAMP THERAPIES WERE SIGNIFICANTLY MORE EFFECTIVE THAN BURST + THERAPIES.

# EFFECTS OF AF SUPPRESSION ALGORITHM ASSOCIATED WITH DUAL - SITE ATRIAL STIMULATION AND $\beta\text{-BLOCKER}$ THERAPY FOR THE PREVENTION OF RECURRENT ATRIAL FIBRIL

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**OBJECTIVES**: To evaluate Optimized Atrial Stimulation, OAS, treatment strategy in the reduction recurrent chronic atrial fibrillation, AF. OAS was defined as dual site atrial pacing, the use of beta blocker and dynamic atrial overdrive, DAO pacing algorithm. Endpoints included quality of life, AF symptom, AF hospitalizations, cardioversions, echocardiography, automatic mode switch, AMS events and Holter monitoring.

BACKGROUND: The use of atrial overdrive algorithms provides another therapy for the reduction of symptomatic AF that can be used in conjunction with pharmacologic and non pharmacologic therapies. METHODS: 25 patients with Sinus Node Disease and recurrent chronic AF received a dual chamber pacemaker with lead placement in the coronary sinus ostium, high right atrium and RV apex. Patients were randomized into two groups: GROUP I DAO ON for three months then crossed over to OFF and GROUP II DAO OFF for three months then crossed over to ON. All patients were programmed to DDDR and started on 100 mg Atenolol/day. Follow up occurred at 3 and 6 months.

**RESULTS**: OAS patients had fewer symptomatic AF episodes per week, (p < 0,001), a larger percentage of atrial pacing (97,8±1,68 and p < 0,001); less AMS activations (61,5±79,0 and p < 0,019); less hospitalizations due to AF (2,85±1,83 and p < 0,001); fewer cardioversions (p < 0,001) and better physical and mental quality of life components index, PCS (53,17±5,5 and p < 0,001); MCS (50,0±4,89 and p < 0,006). **CONCLUSIONS**: The OAS strategy resulting in a reduction in AF episode recurrence, a better QOL and lesser use of hospital resources. Key Words: Dynamic Atrial Overdrive, Optimized Atrial Stimulation, Recurrent Atrial Fibrillation, Atrial Fibrillation Prevention, Dual-Site Atrial Pacemaker Therapy.

#### ECHOCARDIOGRAPHY TO ASSESS CARDIAC RESYNCHRONIZATION

### WHAT IS THE BEST ULTRASOUND PREDICTOR OF CRT RESPONSE IN PATIENTS WITH HEART FAILURE?

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**Background**. Although cardiac resynchronization therapy (CRT) is now used for treatment of dilated heart failure, it is still unclear what is the best mechanical index to predict a favorable response. To address this topic, the multicenter 1-year follow-up EVER-PACING study has been designed. Preliminary data on mid-term 6-month follow-up are presented here.

Methods. Thirty-seven patients (mean age 68±8 years, 27 males) with dilated cardiomyopathy, NYHA class III-IV, left ventricular ejection fraction (LV-EF) <35%, QRS>120 ms were studied before the implantation of the biventricular pacemaker, at predischarge and after 3 and 6 months. Several ultrasound indexes of mechanical dyssynchrony were calculated: conventional Doppler interventricular delay (Qa-Qp, ms), M-mode peak septal to posterior wall motion delay (SPWMD, ms) and wall thickening delay (SPWTD, ms), tissue Doppler standard deviation of 12 time-to-peak systolic LV myocardial velocities (DTI-SD, ms), and standard deviation of 12 time-to-peak systolic LV myocardial strains (Strain-SD, ms). Differences between variables were evaluated by non parametric tests. Predictive analysis was performed by ROC curves with an EF increase of 20% of the baseline values defining responders at 6 months.

**Results**. LV end-systolic volume significantly decreased and EF and dP/dt significantly increased at 3 and 6 months. All ultrasound dyssynchrony parameters significantly decreased over time but only SPWTD, TDI-SD and Strain-SD could differentiate responders from non responders. Strain-SD showed the best accuracy.

Conclusions. Indexes of both interventricular and intraventricular mechanical dyssynchrony are reduced by biventricular pacing, with simultaneous increase of global systolic LV function, indicating effective resynchronization of the heart. Strain-SD, however, seems to be the best predictor of CRT success in terms of LV-EF variation. These results are preliminary and require the 1-year follow-up confirmation.

# ECHOCARDIOGRAPHIC OPTIMISATION OF THE VENTRICULAR-VENTRICULAR INTERVAL INCREASES STROKE VOLUME IN PATINETS WITH BIVENTRICULAR PACING

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Introduction. Cardiac Resynchronisation Therapy (CRT) leads to negative left ventricular remodelling and symptomatic improvement in selected patients (pts) with heart failure. The time delay between right and left ventricular stimulation can be programmed individually and has significant influence on left ventricular synchrony. We hypothesized that echocardiographic optimization of the ventricular-ventricular (V-V) interval leads to improvements of hemodynamics in pts with biventricular pacing.

Methods and results. 11 pts with refractory chronic heart failure and a QRS width >130 msec were evaluated after implantation of a biventricular pacemaker (Insync Medtronic®). Stroke volume (SV), calculated by the continuity equation, was measured at different V-V Intervals (24 msec right before left to 24 msec left before right ventricle) at increments of 4 msec (Table 1). Compared to the standard programmed V-V interval of 4msec, echocardiographic optimization increased SV by 25% from 60±23 to 75 ml±23 (p=0.01, paired t test).

Improvement of SV after echocardiographic optimization could be documented in 8 of 11 pts. A wide interindividual range of optimal V-V Intervals (20 msec left before right to 24 msec right before left ventricle) was observed in the population.

Conclusion. While standard programmed V-V intervals are often suboptimal, echocardiographic optimization significantly increases SV in the majority of pts. The magnitude of this effect is comparable to the benefits of biventricular pacing itself. Since optimal V-V timing shows significant interindividual variation, the optimal V-V interval should be assessed by echocardiography in every individual patient after initiation of CRT.

# LONG TERM EFFECTIVENESS OF CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH ECHOCARDIOGRAPHIC EVIDENCE OF MECHANICAL ASYNCHRONY.

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**Background**: Cardiac resynchronization therapy (CRT) has been proven effective in patients (p) with refractory heart failure (HF) and QRS duration > 120-150 ms. The aim of our study was to evaluate the effectiveness of CRT in p with HF in the presence of echocardiographic evidence of mechanical asynchrony regardless of QRS duration.

**Methods**: 101 p with dilated cardiomyopathy (age 70±10 years, 70% male, 59% ischemic origin), EF < 35% and NYHA 3-4 refractory HF underwent biventricular pacing if inter (aortic-pulmonary Doppler flow delay, IVD) and intraventricular (ECG Q wave-lateral wall contraction delay, Q-LWC) mechanical asynchrony were documented by Doppler echocardiography. All p underwent clinical evaluation, ECG and ultrasound examinations and six-minute walking test (6MWT) at baseline, 1 and 3 months and subsequently every 6 months. **Results**: At follow up (21±12 months) all p demonstrated a significant improvement in clinical and functional data.

	Baseline	Follow – Up	р
NYHA	3,2 ± 0,6	1,8 ± 0,7	< 0,0001
EF (%)	$24,4 \pm 5,5$	$33,9 \pm 6,8$	< 0,0001
LVEDD (mm)	$75,8 \pm 8,6$	$70,3 \pm 9,9$	< 0,0001
LVESD (mm)	$64,1 \pm 8,6$	57,8 ± 10,1	< 0,0001
IVD (ms)	$50,4 \pm 26,3$	11,3 ± 18,7	< 0,0001
Q-LWC (ms)	$426,3 \pm 70,0$	390,5 ± 68,2	< 0,03
6MWT (m)	274,4 ± 86,0	387,1 ± 57,4	< 0,0001
QRS (ms)	156,5 ± 31,2	131,0 ± 22,3	< 0,0001

**Conclusions**: CRT may be considered effective in ameliorating clinical and functional data in p with echocardiographic evidence of mechanical asynchrony regardless of QRS duration.

### THE BENEFITS OF OPTIMIZING THE V-V DELAY IN CARDIAC RESYNCHRONISATION BY DOPPLER INDEX

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The purpose of the present study was to evaluate the performance of the left ventricle (LV) using different V-V intervals. Doppler index of myocardial performance (IMP) has been approved as a non-invasive tool of overall left ventricular function.

#### ECHOCARDIOGRAPHY TO ASSESS CARDIAC RESYNCHRONIZATION

Methods: 8 patients (pts) with dilated cardiomyopathy, NYHA class III or IV, QRS duration range from 100 to 230 msec received a biventricular pacemaker with independent ventricular ports. All pts were at rest and in sinusrhythm. EchoDoppler was used for V-V optimization by IMP (sum of isovolumic times divided by ejection time) with full biventricular capture. The examinations were done at 5 or 6 interventricular delay intervals with steps of 20 msec with either LV lead preactivation or RV preactivation. Pts were investigated before and after pacemaker implantation with a mean follow-up of 5 months. LVEDD, LVEDV, LVESV, EF (LV), IMP and the time interval from the start of the QRS complex to myocardial peak velocity of 6 basal segments of LV were measured. The dyssynchrony index (+ 2SD from the mean of Ts) was calculated.

**Results**: Pre- and Postimplant data are respectively: Dyssynchrony index 73 to 58 (\*), LVEDD 74 to 70 mm (\*), LVEDV 381 to 347 ml, LVESV 301 to 252 ml (\*), EF (LV) 22 to 30%, IMP 0,845 to 0,729 (\*). (\* p < 0.05; mean values are shown).

**Conclusion**: Tailored cardiac resynchronisation therapy with optimal V-V timing by Doppler index may help to improve hemodynamics in pts with chronic heart failure.

#### TAILORED ATRIO-VENTRICULAR AND INTER-VENTRICULAR DELAY PROGRAMMING IN CRT: IS IT CRUCIAL TO OPTIMIZE MYOCARDIAL PERFORMANCE IN HF PATIENTS?

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**BACKGROUND:** Recent development in pacemaker technology enables to program different inter-ventricular delay (VVd) in patients (pts) implanted with a biventricular device. AIM: To evaluate the effects of atrio-ventricular delay (AVd) and VVd optimization on left ventricular systolic and diastolic performance in pts treated with Cardiac Resynchronization Therapy (CRT), measuring the Myocardial Performance Index (MPI).

METHODS: 21 pts (14 m, 69.7 ± 12.7 yrs, NYHA class III/IV, QRS > 130 ms, ejection fraction  $26 \pm 9\%$ ) were implanted with a CRT device (Renewal, Guidant) with programmable VVd. MPI (as the sum of the isovolumetric contraction time and relaxation time divided by ejection time) was evaluated at pre and within 24 hours post implant during simultaneous biventricular pacing (S-BP) and during right or left ventricular pre-activation (20, 40, -20, -40 ms) at different AVds (from 80 to 200 ms by steps of 20 ms). Optimal VVd and AVd combination, identified by the minimum MPI, defined the individual tailored BP (T-BP). RESULTS: Both S-BP and T-BP were associated with a significant decrease in the MPI as compared to baseline (from 1.09  $\pm$  0.41 to 0.78  $\pm$  0.19 for S-BP, p = 0.0004; and to 0.60  $\pm$  0.14 for T-BP, p = 0.00000); a significant difference was also found between the S-BP and T-BP MPI (p = 0.04). The optimal AVd was significantly shorter during right ventricular pre-activation than left ventricular pre-activation (p<0.03). CONCLUSIONS: AVd and VVd optimization is crucial to maximize the myocardial performance evaluated by MPI, in pts treated by BP.

# ECHOCARDIOGRAPHIC AND CLINICAL IMPROVEMENTS IN PATIENTS WITH HEART FAILURE TREATED WITH BIVENTRICULAR STIMULATION: RESULTS ST SHORT AND LONG TERM

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**Background**. Randomized studies demonstrated that cardiac resynchronization (CRT) is a promising therapy to treat patients with heart

failure (HF) and inter-intra ventricular conduction defects. Aim of our study was to analyze short and long term echocardiographic effects in patients implanted with a biventricular system in our center.

Methods. We selected 29 patients (22% male, mean age 69±9 years) with advanced drug refractory HF (NYHA 3.0±0.6), depressed left ventricular function (EF=25.8±5.5%), inter ventricular conduction defects and at least 12 months follow-up (mean 30.5, range 12-48 months). All 29 patients were studied with echocardiography before implantation, at short-term (3 months) and long-term follow-up (at least 12 months) to evaluate systolic and diastolic function and ventricular mechanical delays.

Results. The table reports the most relevant studied parameters

	Baseline	Short term	Long term
Left ventricular filling time (ms)	370,9±109,6	385,1±123,8	440,2±92,3*
Left ventricular telesystolic diam. (mm)	60,2±8,3	55,6±9,9*	53,2±12,8
Interventricular conduction delay (ms)	52,9± 23,8	18,3 ± 20,3*	17,7 ± 21,8
Mitral regurgitation (mm2)	6,5 ± 4,9	4,6 ± 4,8*	4,2±4,1
Ejection fraction(%)	25,8 ± 5,5	31,6 ± 6,8*	33,6 ± 9,6
NYHA class	$3.0 \pm 0.6$	$2,0 \pm 0,5*$	$1,9 \pm 0,5$

**Conclusions**. 1) CRT is effective to improve haemodynamic performances in patients with HF, systolic dysfunction and inter ventricular conduction defects.

- 2) Haemodynamic benefits are observed in both systolic and diastolic phase.
- 3) Most parameters significantly improved at short-term follow-up and benefits persisted at long term follow-up
- 4) Left ventricular filling time improves significantly at long-term, confirming data about CRT benefits on diastolic phase.

# PREDICTIVE VALUE OF STANDARD AND TDI ECHOCARDIOGRAPHIC PARAMETERS FOR THE SELECTION OF CANDIDATES FOR CARDIAC RESYNCHRONIZATION THERAPY

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**Background**. Cardiac resynchronization therapy (CRT) has been demonstrated to be effective in patients (pts) with heart failure (HF) and ventricular dyssynchrony (VD).

The observation of variable efficacy of CRT has resulted in efforts to predict the response to this approach.

Purpose: identification of reliable echocardiographic predictors that can prospectively select the pts who most likely respond to CRT. **Methods.** 158 pts with HF and intra- and inter-VD defined by QRS larger than 150 ms or via standard or TDI echocardiography were implanted with InSync III biventricular PM (Model 8042, Medtronic III).

Inc., USA) in 10 cardiological centers. 50 pts with at least 6-month follow-up (FU) were analyzed. Responders were defined by a composite endpoint: alive pts who had a persistent improvement of at

least 1 NYHA class, without hospital admissions for HF during the follow-up period, and relative increase in LVEF>=25%. The receiver operating characteristics (ROC) curves for sensitivity and specificity were constructed to evaluate the predictive values and accuracy of the studied variables.

**Results**: Comparing baseline and 6-month FU measurements, statistically significant (P<0.01) were observed in NYHA class (from  $3.1\pm0.6$ to  $1.9\pm0.6$ ), in QRS width (from  $157.6\pm29.1$ to  $129.2\pm23.3$ ), in LVEF (from  $24.5\pm7.5$  to  $35.5\pm11.6$ ), in LVEDD (from  $69.2\pm9.7$  to  $66.4\pm11.1$ ), in LVESD (from  $58.6\pm11.5$  to  $54.8\pm11.9$ ).

According to ROC analysis, predictability of responder pts was limited being 66% the positive predictive value (PPV) selecting pts with QRS higher than 150 ms, and being lower than 71% the PPV using several standard or TDI echocardiography parameters.

These preliminary analyses show that in a patient population enrolled in multicenter clinical practice more than 50 pts are needed to find reliable echocardiographic parameters.

Conclusions In pts with CHF and intra- and inter-VD, this prospective study confirms that CRT is effective but questions the possibility to find reliable predictors. Further analyses in a larger population are needed to identify predictors of CRT success.

## A NOVEL METHOD TO ASSESS CARDIAC RESYNCHRONIZATION THERAPY BY THREE DIMENSIONAL ECHOCARDIOGRAPHY

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Criteria for identify dyssynchrony and optimal site for lead positioning are essential for achieving clinical benefit by resynchronization therapy(RT). Recent reports showed that three dimensional echocardiography analysis(3DE) is reliable in assessing regional evaluation of ejection fractions REF and Volume/Time curves.

Purpose of our study is to assess the potential diagnostic informations given by 3DE REF in pts with LBBB and dilated cardiomyopathy with EF < 35% The steps allowing the 3D analysis are the following: fast freehand acquisition automatic endocardial contour, volume measurements AND ejection fractions global and regional, Bullseye display, graph display of regional parameters (Volume/Time curves). The software uses as centerline method the center of gravity which is mobile during the cardiac cycle and on thIS basis calculate all over the cycle a pyramidal volume for any segment which allow regional evaluation of ejection fractions and Volume/Time curves.

Our study group include 15 pts (10 males), two pts underwent RT. Inferior, lateral a posterolateral segment Septal segments were delayed compared to Septal segments (range 10 to 18% of cardiac cycle length), while REF was higher in the inferior, lateral and posterolateral segments. Furthermore a wide range of delays among inferior, lateral and posterolateral segments exist. In the two pts treated by RT, the highest delay was located in different LV segments basal inf and medium PL segment and it was normalized by RT with improvement of regional and global EF.

These preliminary result showed that different synchronicity is a complex phenomen and its assessment by 3DE may be useful in patient selection, lead positioning resulting in better prognosis in RT.

#### CATHETER ABLATION TO CURE ATRIAL FIBRILLATION

## RADIOFREQUENCY ABLATION WITH LINEAR LESION: EFFECTIVENESS IN DIFFERENT PATTERNS OF ATRIAL FIBRILLATION.

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BACKGROUND: Altough pulmonary vein isolation is an established approach in the treatment of atrial fibrillation, recurrences rate is about 30% in the paroxysmal form, increasing up to 40-50% in presence of structural hearth disease and persistent/permanent atrial fibrillation.

Substrate modification with surgically applied linear lesions is associated with a success rate exceeding 90% even in structural hearth disease

Our aim was to evaluate safety and effectiveness of substrate modification by transcatheter left atrial linear lesions.

METHODS and RESULTS: Population: 50 patients, Age 58,Male (74%) Paroxysmal AF 23(42%),Persistent AF 17 (38%), Permanent AF 10 (20%),AF history 4,5, LV ejection fraction 55%, left atrial volume 122 (54-230) ml. Pts were divided into 4 groups:No structural heart disease 28 (56%), Hypocinetic heart disease 10 (20%), Valvular heart disease 10 (20%), Hypertrophyc cardiomyopathy 2 (4%). Procedures were conducted in sinus rhythm and atrial fibrillation.

After transseptal catheterization and during anticoagulation with eparin, the electromagnetic mappingsystem (Carto, Biosense Webster Inc.) was used for reconstruction of the left atrium, pulmonary veins and mitral anulus. Ablation was performed with irrigated tip radiofrequency catheter (temperature limit of 43°C, power between 30 and 50 W). Ablation lines:encircling of the pulmonary veins, mitral anulus-left inferior pulmonary vein istmus, left atrial roof and,in presence of atrial volume grater than 150 ml, a line between the two inferior pulmonary veins. Antiarrhythmic drugs if present at the baseline were discontinued after 3 months.

After a mean follow up of 8,5 months recurrences rate was 34% in the first month. Early recurrences were self terminating or underwent electrical cardioversion and failed to show any influence on late recurrences. The maintenance of sinus rhythm in the follow up was 90%, without differences among the four groups.

Two procedures were complicateted by pericardial effusion without need of drainage.

**CONCLUSIONS**: Substrate modification by transcatheter left atrial linear lesions is safe and higly effective in the treatment of atrial fibrillation both in normal and structural heart disease. Recurrences within the first month after ablation do not influence the late outcome.

# TERMINATION OF PERSISTING ATRIAL FIBRILLATION DURING PULMONARY VEIN ISOLATION – FINDINGS FROM CONTINUOUS MAPPING OF PULMONARY VEINS AND CARTO NAVIGATE

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Findings from pulmonary vein (PV) mapping during PV isolation using electroanatomic (EA) circumferential lesions (CL) in patients (pts) with persisting episode of intermittent atrial fibrillation (IAF) are presented. Methods: Among 145pts (25F), aged 53.2±10.8 years, with IAF and normal heart, 31pts had ablation during AF persisting hours to days. Incessant repetitive AF,AF induced by catheter maneuvers and reablations were excluded. PVs were mapped with a circular catheter, extraostial CL were completed using EA navigation. Full

PV isolation was the procedure end-point. PV were isolated in order: left superior (LS), left inferior (LI), right superior (RI) and right inferior (RI). Results: In 30 pts, PVs exhibited rapid activity, typically ranging between 400 to 600 bpm. During PV isolation, AF either:1) persisted after elimination of potentials in a particular PV;2) terminated, preceded by deceleration of activity in the LA or both PV and LA;3) AF terminated in the LA, while AF/AT persisted in the PV. AF terminated in 26 (84%) pts during PV isolation: 6xLS, 5xLI, 13x RU, and 2x during RI isolation. In 24 pts, AF terminated simultaneously in the PV and LA. In these pts, target PV could often initiate further AF episodes until full disconnection. In 2pts, following PV disconnection and AF termination in the LA,AF/AT persisted confined to a PV.Of these 26pts, 24 (92%) are free of AF in long term. Conclusion:1) PV mapping demonstrates that IAF can be maintained by PV ostial focal or reentry activity.2) CL around PV terminates persisting AF by partial or full PV isolation. 3) Long-term cure of IAF requires full PV isolation in most of the pts.4) Termination of AF required in >50% of the pts isolation of at least 3PVs, hypothetically due to cumulative effect on more firing PVs or elimination of one firing PV in the selected order of isolation.

## ORIGIN AND FUNCTION OF INTRINSIC NEURAL PATHWAYS LOCATED IN THE AREA OF PULMONARY VEINS.

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Origin and function of intrinsic neural pathways located in the area of pulmonary veins.

The aim of present study was to verify topography of intrinsic nervous pathways (NP) located in area of pulmonary veins (PV) and investigate influence to the function of the heart.

**Methods**. In ten electrophysiological studies with mongrel dogs isolation of NP were performed on epicardial surface of the heart in 6 selected zones of PV by using the standard method of RF ablation. Protocol of investigation included recording of heart rate, sinus node (SN) function recovery time, AV conductivity, refractoriness of the atria, AV node and ventricles.

Results. Isolation in superior right side shows effect of decreased sympathetic tone to heart parameters with no reliable changes of parasympathetic tone. Isolation in middle right side heightened effects, whereas in inferior right side no changes were observed. Isolation in left superior side shows markedly decreasing or termination of parasympathetic tone induced by left n.vagus trunk, although parasympathetic action of right n.vagus trunk remain. Isolation in middle/inferior left side produce insignificant diminishing of parasympathetic effect pronounced to function of SN and absent to AV conductivity.

**Conclusions**. 1. In superior area of the right PV localized sympathetic NP mainly influenced to the AV and less to the SN function.

- 2. In superior area of the left PV localized parasympathetic NP entered from left cervical n. vagus trunk, influenced to AV conductivity and refractoriness of ventricles.
- 3. In inferior area of the left PV localized possibly mixed vagosympathetic NP or sympathetic branch altered SN function.

## HRV AFTER CPV RF ABLATION IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION: FOLLOW-UP RESULTS

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#### CATHETER ABLATION TO CURE ATRIAL FIBRILLATION

**Background**: Local denervation induced by circumferential pulmory veins (CPV) radiofrequency catheter ablation (RF)could be related to efficacy of the procedure. We compared heart rate variability (HRV) before and 6-9 months after CPV ablation in pts with and without paroxysmal atrial fibrillation (PAF) recurrences.

**Methods**: 45 highly symptomatic pts with drug refractory PAF underwent RF, using Pappone technique (31 males, age: 55+/-8 yrs). Holter recordings were performed before (H0) and 6-9 months (H1) after the procedure. SDRR, rMSSD in H0 and H1, as well LF, HF and LF/HF in H1 were used.

Results: 6-9 months after RF 17 pts had relapses of PAF (AF+) and 28 pts were free of PAF (AF-). They did not differ in age, gender, heart disease and medical treatment. Whole population did not differ in HRV, mean and minimum HR in H0 vs. H1. Notwithstanding, comparison of HRV (H0 vs. H1) obtained in AF+ and AF- pts revealed them to be remarkably different. SDRR increased after RF in AF- pts from 103+/-24 ms to 136+/-21 ms (p<0.005) while in AF+ pts it did not change (112+/-14 ms vs. 113+/-28, NS), difference in H1 for AFvs. AF+ with p<0.0001. rMSSD in H0 and H1 were similar in AF+ (25+/-6 ms vs. 20+/-5 ms, NS), but in AF- pts significantly higher values were found (21+/-4 ms, 30+/-8 ms, p<0.05), difference in H1 for AF- vs. AF+ with p<0.0001. Remarkable increase in frequency domain parameters in H1 was also observed in AF- vs. AF+ (p<0.005). Conclusions: Patients with successful clinical outcome of CPV RF ablation have significantly higher values of HRV at 6-9 months after the procedure, opposite to those with AF recurrences.

# PROSPECTIVE ASSESSMENT OF LATE CONDUCTION RECURRENCE ACROSS RADIOFREQUENCY LESIONS PRODUCING ELECTRICAL DISCONNECTION AT THE PULMONARY VEIN OSTIUM IN PATIENTS WITH ATRIAL FIBRILLATION

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**BACKGROUND**. In patients with atrial fibrillation (AF) undergoing radio-frequency (RF) electrical disconnection of multiple pulmonary veins (PVs), the incidence of late conduction recurrences has not been systematically determined.

**METHODS AND RESULTS**. Using a prospectively designed multistep approach, we aimed at assessing the correlation between acute achievement and chronic maintenance of electrical conduction block across RF lesions disconnecting the distal tract of the PV in 43 patients ( $52.3 \pm 8.2$  years) with AF. Forty-one left superior (LS), 42 right superior (RS), 25 left inferior (LI) and 9 right inferior (RI) PVs were targeted during 108 EP procedures ( $2.6 \pm 0.5$  per patient). Seventeen patients underwent 2 procedures, 23 patients 3 procedures and 3 patients 4 procedures. During the first attempt, electrical disconnection was achieved in 112 PVs (95.7%). During a next procedure (time interval,  $4.6 \pm 1.9$  months), conduction recurrence was observed in 32 of 39 LSPVs (82.1%), 29 of 40 RSPVs (72.5%), 20 of 24 LIPVs (83.3%) and 7 of 9 RIPV (77.8%). After re-ablation at gap sites, a later procedure (time interval,  $5.1 \pm 2.4$  months) revealed a second recurrence in 13 of 22 LSPVs (59.1%) and 14 of 19 RSPVs (73.7%).

**CONCLUSIONS.** Conduction recurrence across disconnecting RF lesions can be observed in about 80% of cases 4 months after ablation. Following re-ablation, similar recurrence rates are observed 5 months later. This high rate of late conduction recurrence may contribute significantly to AF recurrence in patients undergoing catheter ablation aiming at disconnection of multiple PVs.

## LEFT ATRIAL FUNCTION AFTER CIRCUMFERENTIAL AND LINEAR RADIOFREQUENCY LESIONS IN TREATMENT OF ATRIAL FIBRILLATION

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The purpose of the study was to evaluate morphological and functional parameters of the left atrium (LA) following catheter ablation for atrial fibrillation (AF). Method: Different parameters obtained during transthoracic and transsophageal echocardiography prior to and 1 month after catheter ablation of AF were compared in 26 patients (pts), (5 F), aged 52.8±7.3 (39-66) years. Electroanatomically navigated circumferential lesions were performed in all pts, additional two linear lesions were performed in 21 of the pts and complex linear lesions in the remaining 5 pts. Results: LA long and short axis diameters (mm) acquired from apical view were compared in 22 pts before and after ablation [long axis: 52.4±4.4vs.57±3.8), p=0.18; short axis: 41.2±3.8vs.38.6±4.2, p<0.01]. LA Long axis increased in 12 and short axis in 6 pts. The increase of the LA long axis >5 mm was measured in 4 pts. No 5 mm increase of LA short axis was found. A wave maximum velocity of the transmitral flow (cm/s) was compared before and after ablation in 18 pts (63±12.7vs60.4±15.7, p=0.18) and decreased by >20% in 3 pts. LA appendage maximum outflow velocity (cm/s) was compared in 24 pts (88.5±32.7vs.101±34.3; p=0.06) and decreased by >20% in 2 pts. Fractional shortening of LA (%) measured from parasternal view was compared in 16 pts  $(19.6\pm7.4vs.22.3\pm6.8; p=0.08)$ . This parameter decreased by >20% of its initial value in 3 pts. Stroke volume (ml) was compared in 24 pts  $(70.8\pm19.3\text{vs}.75.9\pm20.3;p=0.13)$  and decreased by >20% in 6 pts. Two of the parameters worsened in 3 pts and three parameters worsened in 1 pt. None of the patients had complex linear lesions. Three of these 4 pts are completely free of AF. Conclusion: Preliminary results demonstrate that extensive circumferential and linear lesions in the LA are not generally associated with deterioration of the LA function 1 month after ablation.

# ANTIARRHYTHMIC AND ANTICOAGULATION TREATMENT AFTER PULMONARY VEIN ISOLATION – RANDOMIZED COMPARISON OF CONVENTIONAL VERSUS ELECTROANATOMICAL APPROACH

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Long-term antiarrhythmic (AA) and anticoagulation (AC) medication was compared in patients (pts) undergoing conventional (Conv) vs. electroanatomic (EA) pulmonary vein (PV) isolation. Method: 110 pts (21 F), aged 52±10,8 (21to74) years, with structurally normal hearts, were randomized to Conv (Group I -54 pts) and EA (Group II -56 pts) PV isolation. Groups I and II did not differ in atrial fibrillation (AF) occurrence (93%vs 89% of pts > once a week), ineffective AA drugs/pt (4.4±1.4vs.4.2±1.4) and use of amiodarone (Amio) (57%vs.52% of pts), and other characteristics. AA and AC was maintained at least 6 weeks to 3 months and than discontinued according to clinical outcome. Patients' history, standard and Holter ECG were regularly taken. Results: After 3,6,9,12,18, and 24 months (mo) - in Group I 54,54,54,48,36, and 18 pts, resp. in Group II 56, 56, 56, 48, 29, and 19 pts were examined. During 20±8.5 (9-40) mo follow up, 12 resp. 8 reablations were done in Groups I resp. II. AF-free clinical outcome in Group I vs. II was 80 vs. 84%; 81 vs. 84%; 83 vs. 83%; 86 vs 86%; and 83 vs. 95% at mo 6, 9, 12, 18, and 24 (p=NS). Clinically significant AF-free outcome in Group I vs. II was 85vs.93%; 89vs.93%; 92vs.94%; 89vs97%; and 83 vs. 95% (p=NS). Class I or III AA drugs in Groups I vs. II were taken by 44vs.43%; 31vs.20%; 25vs.21%; 25vs.31%; and 28vs.32% of pts after 6,9,12,18 and 24 mo (p=NS). Amio was

used by 20 vs. 7%; 11 vs 5%; 13 vs.2%; 14 vs 0%; 11 vs.0%; and 14 vs.0% (p=NS). AC was taken in Groups I vs. II by 20vs.21%; 15vs.13%; 17vs.8%; 17vs.3%; and 22vs.5% of pts (p=NS). Conclusion: In long-term, EA navigated PV isolation is associated with trend to lower occurrence of clinically significant AF and lower need for Amio and AC medication.

## ABLATION OF ATRIAL FIBRILLATION USING A NEW 8 MM TIP CATHETER WITH 4 THERMOCOUPLE SENSORS AND BASKET

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**Introduction**: In order to treat atrial fibrillation (AF) by radiofrequency (RF) ablation different approaches have been proposed. In this paper we describe our experience using a new multisense 8 mm tip catheter.

**Methods**: 24 patients, mean age 62 years, underwent AF ablation. The procedure end point was PV and superior vena cava (SVC) insulation and right flutter lesion. In order to achieve PV block, very long lesions in LA tissue were performed. PV and SVC were mapped using a 31 mm basket catheter with 64 electrodes. The lesions were performed by a new 8 mm tip bi-directional steerable catheter, carachterized by 4 thermocouples located in the tip. One sensor is on the distal portion of the electrode and three around the proximal electrode extremity. RF energy was delivered during temperature control, at 60 C° at maximum power of 60 Watts. The system is lead by the sensor that achieves the highest temperature to avoid excessive heating on small electrode areas. No complications occurred.

**Results and discussion**: Complete conduction block in 4 PV was obtain in 20 patietns (83%). During a short term follow up (mean  $4\pm2$  months) only 6 patients (25%) experienced recurrence of AF. There is some concern in using a 8 mm tip catheter with high voltage setting in the LA because of embolic risk. We never documented thrombus on the electrode (even after high voltage delivery) using the multisense catheter.

**Conclusions**: A 8 mm multisense catheter could be an appropriate and safe tool in order to perform long linear lesions in the LA. The catheter manipulation appear to be easier compared to available cooled 4 mm tip catheters.

#### CARDIAC RESYNCHRONIZATION THERAPY

## THE RESYNCHRONISATION THERAPY IN SEVERE CONGESTIVE HEART FAILURE: EFFECTS ON NEUROHORMONAL ASSESSMENT

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Biventricular pacing in patients with severe congestive heart failure (CHF) and complete left bundle branch block (LBBB) reduces the NYHA class improving quality of life. The aim of the study was to assess the effect of biventricular pacing on neurohormones brain natriuretic peptide (BNP), aldosterone (ALDO), endothelin1 (E1), big-endothelin (BigE) and TNFalfa.

Methods: 51 CHF patients (32 males) underwent implantation of biventricular pacemaker and plasma determination of neurohormones at baseline and at 9-month follow-up. Patients included had complete LBBB (QRS>140 ms), left ventricular ejection fraction (LVEF)<30% and NYHA III-IV. The causes of CHF were: dilatative cardiomyopathy in 55%, CAD in 33%, valvular heart disease in 8% and hypertensive in 4%. The neurohormonal plasma determination was obtained with immunoradiometric assay. The dosage of carvedilol, digoxin and enalapril remained unchanged during the study period; only the dosage of furosemide was reduced (baseline 47.7 mg/die vs FU 30.5 mg/die, p=0.006).

**Results**: the PM implantation was successful in 49/51 subjects, mean age 69+-7. The functional class improved at 9-month follow-up (NYHA class from 3,15+-0,49 to 1,15+-0,49 p=0.001). The results of neurohormones are depicted in table 1.

**Conclusions**: biventricular pacing improves the NYHA class in severe CHF patients (p=0.0001). The resynchronisation therapy reduces BNP and BigE (p=0.032 and p=0.007, respectively) without modifying TNFalfa and E1.

### EVALUATION OF THE IGF-1 IN PATIENTS WITH HEART FAILURE AND BIVENTRICULAR PACING

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**Purpose**: Insulin-like growth factor 1 (IGF-1) seems to be related to the disease progression in heart failure (HF) patients. Cardiac resynchronization therapy (CRT) is now widely used in this population to improve clinical conditions, to achieve reverse remodeling and to restore the neurohumoral balance. To date, the potential effect of the CRT on IGF-1 changes has not been explored. Study aim was to evaluate the IGF-1 modifications at baseline, before CRT, and at 3 months follow-up.

Methods: Preliminary data on 18 patients (14 males, mean age 70+/-10 years), with cardiomiopathy of any etiology and optimal drug therapy were analyzed. All patients had ventricular dissynchrony assessed by Echocardiography and QRS duration greater than 130 msec (174+/-14 msec). Baseline measurements included clinical history, physical and functional examinations by means of echocardiography and 6 minute walking test (6MWT). Samples of IGF-1 and Interlouchina-6 (IL-6) were drown.

**Results**: A Wilcoxon non parametric paired test was used. A statistically significant improvement was found at 3 months follow-up for QOL (N=18: 13,5+/-12 vs. 33,2+/-14; p=0,0002), IGF-1 (N=18: 174,6+/-111 ng/ml vs. 136,6+/-79; p=0,0385), IL-6 (N=18: 36,7+/-47 vs. 68,4+/-46; p=0,0030), LVEF (N=18: 33,1+/-10 vs. 29,2+/-7; p=0,0406), NYHA Class (N=18: 1,9+/-0,8 vs. 3,0+/-0,5; p=0,0009), while 6MWT (N=10: 361,2+/-102 m vs. 289,8+/-111; p=NS) was not statistically significant.

**Conclusions**: CRT in severe HF patient population seems to favorably affect the IGF-1 levels, with improvement in QOL for the pa-

tients. We could speculate that higher levels of IGF-1, beside the already known CRT hemodynamic effects, may have additionally benefits on the functional capacity through a growth in muscular tissue. Longer follow up and additional patients are needed to consolidate results.

# REDUCTION OF CIRCULATING ADRENOMEDULLIN LEVELS IN SEVERE CONGESTIVE HEART FAILURE PATIENTS SUCCESSFULLY TREATED WITH RESYNCHRONISATION THERAPY

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Adrenomedullin (AM) is involved in the regulation of cardiovascular homeostasis and has a role in the pathophysiology of heart disease. Circulating AM concentrations are elevated in patients (pts) with congestive heart failure (CHF) in proportion to severity of cardiac impairment. Resynchronisation therapy (RT) has been reported to improve NYHA Class and quality of life (QOL) in selected patients with severe CHF.

Aim of this study was to assess whether RT may determine changes in circulating AM levels in pts with NYHA Class III-IV CHF.

In 15 pts under RT, 8 males, mean age 67 years, AM levels were assessed before and at 8 months (range 4-15) after pacemaker implantation. AM levels showed an important although not statistically significant decrease from  $33.7 \pm 8.2$  pmol/l at baseline to  $21.3 \pm 2.6$  pmol/l at follow-up.

Pts were divided in two groups: GI (10 pts) who showed >1 improvement in NYHA Class and Minnesota QOL (from 73  $\pm$  3 to 60  $\pm$  4, p<.05) and G II (5 pts) who did not show changes in NYHA Class and QOL (from 73  $\pm$  6 to 69  $\pm$  5). The two Groups were comparable for medical treatment and ventricular ejection fraction (LVEF) at baseline. A significant decrease in AM levels was observed in GI; conversely, in GII an increase in AM levels was reported (Delta= -21  $\pm$  8.8 vs 8  $\pm$  1.8, in GI and GII, respectively; p<0.05). A modest increase in LVEF was observed in GI and GII (14 $\pm$  5%, vs 12  $\pm$  6%).

These preliminary data show that RT-induced improvement in NYHA Class and QOL is associated to decrease in AM levels. Thus, RT can modify AM circulating levels, which may - in turn - contribute to clinical improvement of severe CHF pts.

## T WAVE ALTERNANS THRESHOLD AND NT-PRO-BNP IN HEART FAILURE PATIENTS WITH INDICATION FOR CARDIAC RESYNCHRONIZATION

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Purpose: Evaluation of NT-pro-BNP and T wave alternans (TWA) threshold in pts with indication for cardiac resynchronization (CR). Material and Methods: 30 pts (15 with dilatative (DCM) and 15 with ischemic (ICM) cardiomyopathy, all in NYHA III, on optimized medical therapy and with intraventricular dyssynchrony) were studied before CR. Pts with renal failure (creatinine >2.0 mg/dl) were excluded. Firstly NT-pro-BNP was measured (Elecsys 2010, Roche); then TWA (Cambridge Heart, USA) increasing atrial pacing rate (APR): 90, 100, 110 bpm (each step 3 min). TWA positive: if sustained higher than 1 min, with amplitude higher than 1.9mV and alternans ratio higher than 3 in the vector magnitude lead, any orthogonal lead, or 2 consecutive precordial leads. Results: TWA was positive in 12 DCM and in 9 ICM. TWA amplitude increased progressively in pts positive at 90 bpm (8 DCM and 4 ICM) reaching the maximal value

(always in precordial leads) at 110 bpm. These parameters (mean±1SD) were evaluated for DCM and ICM: NT-pro-BNP (1930±1769 vs 11396±12540 pg/ml); TWA maximal amplitude (11.6±6 vs 8±5  $\mu$ V); QRS (148±30 vs 121±31 ms); EF (35±9 vs 35±9%); left ventricular enddiastolic (198±82 vs 193±77 ml) and endsystolic (131±68 vs 132±76 ml) volumes; deceleration time (221±96 vs 201±68 ms); E-wave peak velocity (74±26 vs 72±26 cm/sec); A-wave peak velocity (46±37 vs 50±22 cm/sec), age (75±5 vs 76±5 yrs). Comparing DCM and ICM only NT-pro-BNP was significantly (p < 0,007) higher in ICM. Conclusions: 1) TWA amplitude increases augmenting APR. Identification of pts with positive TWA at lower APR is important for prognostic evaluation. 2) NT-pro-BNP, when left ventricular function does not differ, is higher in ICM pts. 3) Precordial leads are unique for evidencing TWA maximal amplitude.

### MECHANICAL AND ELECTRICAL ALTERNANS IN HEART FAILURE PATIENTS IMPLANTED WITH BIVENTRICULAR PACEMAKERS

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Purpose: noninvasive and simultaneous evaluation of mechanical alternans (MA, i.e.: pulsus alternans, evaluated so far invasively) and of T wave alternans (TWA) to control: a- if they coexist in heart failure (HF) patients, b- modalities of MA appearance. Materials and Methods: 15 patients (7 with dilatative and 8 with ischemic cardiomyopathy; age 62.8±12.3; 11 males; EF=30±5%; all in NYHA class III, with intraventricular dyssynchrony, and on optimized medical therapy) who underwent implantation of a biventricular pacemaker (BP) were studied. MA (constant alternating pressure >4 mmHg lasting more than 20 beats) was evidenced analysing pressure wave by Most Care (PRAM Method FIAB by BIO-SI, Italy) obtaining analogic signal by Finapres (Ohmeda, MA). Most Care analysing beat-to-beat pressure wave morphology furnished also hemodynamic data (trends of: systolic pressure, cardiac cycle efficiecy, stroke volume, and dP/ dt). TWA (positive when sustained for at least 1 min. with an onset heart rate less or equal than 110 beats/min, alternans amplitude higher than 1,9 mV, and alternans ratio higher than 3 in the vector magnitude lead, any orthogonal lead, or two consecutive precordial leads) was evaluated by a dedicated poligraph (Cambridge Heart, Inc., Bedford MA, USA). MA and TWA were evaluated simultaneously one week after BP implantation during DDD pacing (110 bpm, AV interval 120 ms) for at least 5 min. Results: MA and TWA were present simultaneously in 10 patients (absent in the other 5 patients). MA was induced, in the 10 patients, even by spontaneous extrasystoles. Conclusions: Our data indicates that MA and TWA coexist in HF patients. Further studies are necessary to evaluate if they have a common mechanism and/or the same value for prognostic and therapeutic evaluations.

#### EVALUATION OF RESYNCHRONIZATION PATTERN IN BIVENTRICULAR PACING BY RADIONUCLIDE VENTRICULOGRAPHY

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Biventricular pacing (BV) is a well establishes therapy for chronic heart failure (CHF). Some patients show good response to BV (R) whereas others are non responders (NR).

The aim of the study is the evaluation of effective resynchronization obtained with BV.

Method. Patients in sinus rhythm and preserved spontaneous atrio-

ventricular (AV) conduction were evaluated six months after BV. In the same day an equilibrium gated blood pool radionuclide angiography (RNA) acquired during effective BV pacing (BV on). The device was then programmed to a longer AV delay to maintain a spontaneous AV conduction without any fusion (BV off) and 3 to 4 hours later a new RNA was acquired. The contraction pattern was evaluated by phase image analysis as the standard deviation of the mean phase of the left ventricle (SDP) expressed in msec; regional ejection fraction (REF) was also evaluated. Patients were classified as R if NYHA class was reduced al least of 1 class and if in the preceding 6 months patients were not readmitted for CHF.

**Results.** R showed a greater number of left ventricular segments with improved REF during BVon (4.2+/-2.1 vs 1.3+/-1.1). The difference in SDP between BVon and BVoff was greater in R than in NR (105+/-45 vs 45+/-35).

**Conclusion**. RNA phase analysis can identify patients with improved ventricular synchronization achieved with effective biventricular pacing

### BNP AND TWA FOR A MORE ACCURATE STRATIFICATION OF ARRHYTHMIC RISK IN PATIENTS ELIGIBLE FOR CRT

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Aim of the study is to evaluate if BNP and TWA can better identify, in patients needing CRT, those who must receive ICD.

Eight pts. suffering for refractory CHF were evaluated (NYHA III-IV, ischaemic or idiopathic DCM, average EF=22%, with inter/intraventricular asyncronisms).

BNP was measured before, 3 and 6 months after implantation. Three of them underwent TWA analysis, with a positive result. According to Companion trial all pts. received ICD plus CRT.

All pts. underwent: clinical and echocardiographyc evaluation, device controls, BNP and HRV analysis.

**Results**: all pts. improved their functional class, EF, BNP (reduced) and HRV (increased) due to the favourable effect of CRT. Nowadays (average follow-up: 4 months) no malignant arrhythmias conditioning ICD discharges occurred.

Conclusions: as already known CRT significantly improves symptoms and haemodinamyc conditions in severe CHF. The dramatic reduction of basal BNP values well correlates with haemodinamyc restoration. The shortness of follow-up does not allow, at the moment, to foresee a relation between arrhythmic risk and BNP (or its changes) and basal TWA. Nevertheless we hope that the data of follow-up can support the property of a more selective arrhythmic risk stratification (and subsequent ICD implantation) based not only on EF.

# CARDIAC RESYNCHRONISATION THERAPY: CORRELATION BETWEEN PEAK ENDOCARDIAL ACCELERATION AND AORTIC VTI OBTAINED BY STANDARD ECHOCARDIOGRAPHY MEASUREMENTS

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Background: The Aortic VTI (AoVTI) is one of the standard parameters measured during echocardiography (ECHO) procedure to check the efficiency of the ventricular function in heart failure (HF) patients. Selection of Optimal Atrio-Ventricular Delay (OAVD) also improves hemodynamic efficiency of cardiac resynchronisation therapy (CRT). Previous studies demonstrated that Peak Endocardial Acceleration (PEA) allows the OAVD determination in AV block patients

#### CARDIAC RESYNCHRONIZATION THERAPY

(pts). Aim: To verify the correlation between PEA and AoVTI, in HF pts, comparing parameters values in Right V and BiVentricular (BiV) pacing configurations. Methods: 21 HF pts (15 m, 74±7.7yrs, QRS 161±6.8ms, PR 221±16.6ms, NYHA class 3.2±0.38, LVEF 23±6.7%, LVEDD 66±6.6ms) were implanted with a CRT Living CHF system (Sorin Biomedica CRM, Italy), equipped with a PEA sensor. PEA and ECHO measurements were performed in DDD mode (paced condition) with different pacing configurations (Right V, BiV with 0 VV Interval (VV), BiV with compensated VV (Aortic Pre-Ejection Interval - Pulmonary Pre-Ejection Interval)). ECHO measurements have been taken for each pacing configuration at 1 week and after 3 months. For each pacing configuration, the OAVD has been set and the BiV configuration has been compared with Right V pacing. Results: 71% of pts responded to CRT with increased AoVTI in BiV pacing. PEA values in responder pts were 0.45±0.14 g in Right V, 0.60±0.18 g in BiV (p=0.001). A statistically significant correlation was found between percentage variations of PEA vs. AoVTI for all the pts comparing BiV and Right V pacing configurations (r=0.87, p=0.0002 at 1 week, r=0.81, p=0.0024 at 3 months).

**Conclusion**: Variations of PEA values measured by the device and AoVTI obtained by ECHO significantly correlate in CRT patients. Results confirm that PEA is a valid tool for monitoring left ventricular function also in CRT patients.

#### ATRIAL FIBRILLATION PREVENTION BY PHYSIOLOGICAL PACING

### EFFECTIVENESS OF DDD+ OVERDRIVE ALGORITHM IN RECURRENT ATRIAL FIBRILLATION SUPPRESSION

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Atrial Fibrillation (AF) suppression has become the most important target in electrophysiology research, regarding its higher morbidity and mortality association. Recently, new algorithms are able to ensure atrial pacing slightly over the intrinsic rhythm in order to maintain continuous atrial stimulation with percentage above 95 percentage. Objective: To validate the algorithm DDD+ (Philos DR Biotronik) helpfulness in the reduction or even suppression of AF episodes recurrence. Methods: This study was prospective, randomized, controlled, and single blinded and crossover, which has included patients (P) with paroxysmal or persistent AF and symptomatic bradycardia associated. 80 (P) were randomized into two groups (Group I DDD mode in the first 6 months and DDD+ mode in the last in 6 months and Group II DDD+ mode in the first 6 months and DDD mode in the last 6 months). First evaluation in one month after the implant, the second in 6 months and the third, after the crossover in 12 months. They have been evaluated based on 24h Holter, Echo-Dopplercardiography and pacemaker telemetry. Statistical analysis were supported by T Student Test, ANOVA, Pearson Correlation and Wilcoxon Rank Test. Results: The algorithm DDD+ showed better performance than DDD as it could be observed in the following pa-

Echocardiogram		Telemetry	
Left Atrial Size	p<0.001	Atrial Pacing	p<0.01
Diastolic Function	p<0.01	Atrial Fibrill. Episodes	p<0.05
Holter		AES per HOUR	p<0.01
SVE per 1000	p<0.001	Atrial Tachycardia	p<0.01
SVE TOTAL	p<0.001	Automatic Mode Switching	p<0.01
SV tachyarrhythmia	p<0.001		

**Conclusions**: The overdrive atrial stimulation clearly has decreased the AF episode number and improved the diastolic ventricular function as well as atrial size, indicating its electrical and structural reverse remodeling.

**Key word**: Overdrive Atrial Stimulation; Atrial Fibrillation; Automatic Mode Switching; DDD+ Algorithm.

# WHAT ARE THERE THE MAIN PREDICTORS OF ATRIAL FIBRILLATION RECURRENCE IN ELDERLY PATIENTS WITH SICK SINUS SYNDROME AFTER DDD PACEMAKER IMPLANTATION.

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**Background**: It is estimated that majority of the pacemaker (PM) recipients are elderly patients (pts). Dual chamber pacemaker (DDD PM) in the elderly is still controversial because of its short life expectance and the high risk of AF.

The aim of the study was to evaluate factors which can predict persistent AF (persAF) (requiring electrical cardioversion (DC) in elderly (pts) with sick sinus syndrome (SSS) after DDD PM during 1 year follow-up (1yFU).

**Methods**: 50 pts with, with mean age 79,6±4 years implanted with DDD PM DDD during the mean follow up 15±3,2 months with SSS were estimated. Following clinical and electrical parameters were compared between pts who devoloped persistent AF (persAF) (Gr I)

and pts without persAF (Gr II) during 1 yFU: age, history of frequent AF episodes (defined as more once a week), hypertensio, diabetes mellitus, coronary artery disease, history myocardial infarction, stroke, valvular disease, heart failure in class IIIorIV, left atrial diameter (LAd), left ventricle ejection fraction (LVEF), P wave duration (Pdur). **Results**: In 13 pts (27%) persAF was found. In 7 pts (14%) successful DC was performed. 6 pts (13%) were not able to convert to sinus rhythm. Number of frequent episodes before implantation was significantly higher in 13 pts with pers AF comparing to pts with sinus rhythm: (GrI=12pts (92%)vsGrII=6pts (16); p=0,001). Additionally the value of Pdur and LAd was significantly higher in pts with pesrAF (Pdur: GrI=120±22,7msvsGrII=91,7±15,2ms; p=0,03 and LAd: GrI=51±1,1mmvsGrII=43,4±0,5mm; p=0,026 respectively). There was no significant differences between two groups in all others factors.

**Conclusions**: In elederly pts with SSS after DDD PM implantation previous frequent AF attacks, increased P wave duration and left atrial diameter were significantly associated with persostent AF episodes during 1 year follow up.

## A META-ANALYSIS OF TRIALS ASSESSING EFFECT OF PACING MODE IN PATIENTS WITH ANTIBRADYCARDIA PACING

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**Objective**: Retrospective studies reported that physiologic pacing compared to ventricular pacing reduces development of chronic atrial fibrillation, stroke and cardiovascular mortality in patients with sinus node disease or complete heart block. Randomised prospective studies (including large trials) testing hypothesis on benefits of physiologic pacing on mortality did not yield conclusive results. Metanalyses are now widely used to provide evidence to support clinical decision making or to show the need for further research. The aim of this study was to assess the influence of pacing mode on survival and risk of atrial fibrillation in patients with atrioventricular block or sinus node disease.

**Methods**: Studies were selected using MEDLINE database and experts consultations. Results of five randomized, controlled trials were included into analysis. Data were extracted from published materials and odds ratio for death from all causes and for incidence of atrial fibrillation were calculated. A random-effects model was used to quantify the average effects of physiologic pacing (defined as atrial or dual-chamber pacing) on survival and on risk of atrial fibrillation

Results: There was a highly significant heterogeneity between studies results (p<0.0001). In five trials (5408 patients) the effect of physiologic pacing was associated with odds ratio [OR] 0.73 (95% confidence interval [CI], 0.64 to 0.83) for death from all causes. Analysis of patients with sinus node disease revealed more benefits of physiologic pacing compared to ventricular pacing: OR 0.62 (95% CI, 0.5 to 0.79). OR related to physiologic pacing calculated only for patients with atriovevtricular block (data from two studies) was not significantly associated with better prognosis: odds ratio 0.85 (95% CI, 0.61 to 1.19). Assessing the risk for atrial fibrillation for all patients physiologic pacing was also associated with better outcome (OR 0.8 (95% CI, 0.74 to 0.87). Conclusion: These results support a general recommendation to use physiologic pacing in the treatment of symptomatic sinus node disease. However, results from this meta-analysis are not in accordance with the results of the largest trials CTOPP (The Canadian Trial of Physiologic Pacing, 2568 patients) and MOST (Mode Selection Trial in Sinus Node Dysfunction, 2010 patients) that showed small or even no benefit on survival.

#### SINUS RHYTHM BEGETS SINUS RHYTHM IN BRADY-TACHY SYNDROME PATIENTS IMPLANTED WITH DDDRP PACEMAKERS

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**BACKGROUND:** RECENT OPTIONS TO TREAT ATRIAL TACHYARRHYTHMIAS (ATA) INCLUDE THE USE OF IMPLANTABLE PACEMAKERS DELIVERING PREVENTIVE PACING AND ANTITACHYCARDIA PACING THERAPIES (DDDRP-PM).

**AIM OF THE STUDY**: EVALUATE LONG TERM ATA TEMPORAL EVOLUTION IN PATIENTS WITH BRADY-TACHY FORM OF SINUS NODE DISEASE (BT-SND) AND IMPLANTED WITH A DDDRP-PM.

METHODS AND RESULTS: 346 BT-SND PATIENTS WITH PRIOR HISTORY OF ATA RECEIVED A DDDRP-PM AND WERE FOL-LOWED FOR A MEDIAN FOLLOW UP OF 19 MONTHS. SEVERAL ATA ENDPOINTS SHOWED SLOW BUT SIGNIFICANT TRENDS TOWARD SINUS RHYTHM MAINTENANCE AS A FUNCTION OF TIME: THE PERCENT OF PATIENTS WITH ATA-RELATED HOS-PITALIZATIONS DECREASED AT RATES OF 0.1% PER MONTH, THE PERCENT OF PATIENTS WITH ATA RECURRENCES LONG-ER THAN 1 HOUR AT 0.3% PER MONTH, THE PERCENT OF PA-TIENTS WITH ATA RECURRENCES LONGER THAN 1 DAY AT 0.2% PER MONTH, THE PERCENT OF DAYS WITH ATA RECUR-RENCES LONGER THAN 1 HOUR AT 0.1% PER MONTH. ATA EPISODES BECAME SIGNIFICANTLY SLOWER AS A FUNCTION OF TIME: AT EACH FOLLOW-UP MONTH ATA CYCLE LENGTH WAS ON AVERAGE 0.7 MS SLOWER THAN THE PREVIOUS MONTH

AT BECAME PERMANENT IN 2.4% OF PATIENTS PER YEAR. STROKE OCCURRED WITH A 0.55% ANNUAL INCIDENCE. CONCLUSIONS: OUR DATA SUGGEST THAT DDDRP PACING IN PATIENTS WITH BT-SND MAY SUPPRESS ATA AND INDUCE A SLOW PROCESS OF REVERSE ATRIAL ELECTRICAL REMODELING.

# SEASONAL VARIATION OF ATRIAL TACHYARRHYTHMIAS ACCORDING TO GEOGRAPHICAL ORIGIN OF BRADYCARDIA PATIENTS IMPLANTED WITH ANTITACHYCARDIA PACEMAKERS

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**Purpose**: Evaluation of seasonal variation of atrial tachyarrhythmias (AT) considering asymptomatic episodes and above all geographical distribution of patients. The new pacemakers with extended monitoring capabilities allowed us this analysis. Material and Methods: 445 consecutive pts (224 males, age  $71.3 \pm 8.7$  yrs) were prospectively enrolled and implanted with a DDDRP pacing system (AT500 model, Medtronic, Inc.). Results: Data from the first year after implant evidenced for all patients a significant seasonal variation (r = 0.621) with 2 peaks (in December and in June). Different behaviours were evidenced dividing Italy into three geographical areas. Northen (r = 0.367) and central (r = 0.283) parts of Italy had a behaviour with 2

peaks like those of all patients, while the southern part (r = 0.809) of Italy evidenced only a winter peak. Conclusions: Climatic and environmental differences among geographical areas could explain our results. Our data indicate that geographical origin of pts and period of observation appear relevant when performing AT therapy studies.

## ATRIAL MEASUREMENTS AT IMPLANT AND INCIDENCE OF ATRIAL FIBRILLATION IN PATIENTS WITH SSS AND IN PATIENTS WITH AV BLOCK

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Aim of the study is to evaluate atrial pacing threshold, P wave amplitude and incidence of atrial fibrillation (AF) in two populations of pacemaker patients (pts): group A with isolated AV block and group B with SSS (isolated or associated to AV block). Methods: we have reviewed data of pts implanted from April 2003 to April 2004, excluding VVI and VDD pacemaker pts, tri-chamber pacemaker pts without conventional indication to pacing, and pts with a possible structural malfunction of the atrial catheter. Results: 119 pts were enrolled. Group A: isolated AV block, 59 pts, 33 males, 26 females, age 79.7±8.5; Group B: SSS, 60 pts, 32 males, 28 females, age 75.7±8.2. Age difference between group A and B is significant (p<0.05). The two groups are comparable as to types of electrodes and site of implant (bipolar, right atrial appendage). There were no significant differences in atrial pacing threshold (group A 0.57±0.34 V, group B  $0.65\pm0.42$  V, p=NS). P wave amplitude was higher in group A (5.12±2.4 mV) than in group B (4.17±2.11 mV) (p<0.05). Only 2 pts in group A (3.4%) reported AF episodes before implant vs 22 pts (36.7%) in group B. Similarly, in post-implant follow-up (FU) only 4 pts in group A (6.8%) had clinically documented AF vs 21 pts (35%) in group B. P wave amplitude was significantly lower in pts of either group who developed AF (3.90±1.99 mV) vs pts who did no develop AF (4.90±2.34 mV) (p<0.05). Conclusions: as expected, pts with SSS developed AF in the FU more frequently than pts with isolated AV block. P wave amplitude was significantly worse in pts with SSS than in pts with isolated AV block. Pts, who developed AF in FU, independently of underlying disease, had lower P wave amplitude at implant.

#### SUDDEN DEATH RISK STRATIFICATION

### DISPERSION OF QRS COMPLEX, QT AND TRANSMYOCARDIAL REPOLARISATION AS SUDDEN

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The aim of study: evaluation of dispersion of QRS complexes, QT and transmyocardial repolarisation in prediction of sustained ventricular arrhythmias inducibilty during programmed electrical stimulation (PES) in pts after myocardial infarction in relation to sudden death risk assessment.

We observed 32 pts. (24 male,8 female) aged 39-67 yr. after MI, referred to PES. Sustained monomorphic ventricular tachycardia (smVT)or ventricular flutter/fibrillation (VF) were induced during PES in 13 pts - Group I. In this group 8 pts had induced smVT (subgroup IA) and 5 pts - VF (subgroup IB) Standard PES did not induce of any sustained VT or VF in 19 pts - Group II. Left ventricle ejection fraction (EF) was evaluated by echocardiography examination in all pts. The following parameters were assessed based on 12-lead ECG registered prior to PES: max QRS duration, QRS dispersion (QRSd)measured as difference between max and min QRS duration, QT, QTc, QT dispersion (QTd)and transmural dispersion of repolarisation (t-QTd) was measured as an averaged value of peak to end distances of T wave in leads V5 and V6.

**RESULTS:** Left ventricle dysfunction (EF 45%  $\pm$ 11%) was noticed in all pts. Res Higher values of QRS(119,54 vs 101,79ms), QRSd (39,23 Vs. 22,48 ms)and t-QTd (76,54 vs. 62,76 ms) were observed in pts with induced sustained ventricular arrhythmias, particularly monomorphic VT, whereas there was no differences of QT, QTc and QTd between group l, IA,IB and II.

#### **CONCLUSIONS:**

- Higher values of QRS duration and dispersion as well as transmural QT dispersion could predict inducibility of complex ventricular arrhythmias in post-MI patients.
- QRS duration, QRS dispersion and transmural dispersion of repolarisation may be useful in SCD risk stratification after MI.

## IS MICROVOLT T-WAVE A RELIABLE MARKER OF SUDDEN CARDIAC DEATH IN PATIENTS WITH PACEMAKER OR IMPLANTABLE CARDIOVERTER/DEFIBRILLATOR?

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**Introduction**: Microvolt T-wave alternans (MTWA) is becoming a valid non invasive test for sudden cardiac death risk stratification. The measurement of MTWA has recently been demonstrated to be a powerful non-invasive predictor of the risk of ventricular tachyarrhythmias and sudden cardiac death in a number of different patient populations.

**Methods**: A total amount of 64 patients were enrolled for this study. All the patients were evaluated for MTWA, through the use of Cambridge-Heart, Heart Twave System, High resolution electrodes and specific PM/ICD programmers. Alternans was considered significant, and a test was referred at as positive, when alternans was present between 90 and 110 bpm, for more than 2 minutes in two consequential precordial lead, or in one peripheral.

Results: At the first control 3 of the 35 patients with pacemaker (PM) and 15 of the 29 with implantable cardioverter/defibrillator (ICD) were positive for MTWA. At the 18 months follow-up, 6 episodes of ventricular tachycardia (VT) and 3 of ventricular fibrillation (VF) were recorded by the device in 9 of patients with ICD. At Kaplan-Meier analysis, MTWA showed as a highly significant predictor of clinical arrhythmic events in all patients studied (p<0,05).

**Conclusion**: This study demonstrates that TWA is an accurate predictor of SCD in patients with PM and ICD.

### T WAVE ALTERNANS AND ARRHYTHMIA INDUCIBILITY IN POST AMI PATIENTS

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Left ventricular ejection fraction is accepted as a significant risk factor for Sudden cardiac death (SCD). Microvolt T wave alternans (MTWA) has proved useful for screening the risk of SCD. However, MTWA is positive in 40-50% of patients with LVEF < 30%.

Methods and results: 52 post acute myocardial infarction (AMI) patients, LVEF > 40% were screened through exercise MTWA. No patient had any documented prior ventricular arrhythmias. MTWA was positive in 17 patients (35%). 14 MTWA positive patients were further stratified by programmed ventricular stimulation (PVS). Rapid monomorphic ventricular tachycardia was induced in 6 patients (42,8%).

**Conclusion**: These preliminary data show that presence of MTWA is associated with ventricular arrhythmia inducibility on PVS in post-AMI patients with LVEF > 40%. If post AMI patients with LVEF > 40%, MTWA positive and inducible ventricular tachyarrhythmias on PVS must be implanted with an ICD, remains a clinical challenge.

### CALCIUM CHANNEL BLOCKERS INFLUENCE T WAVE ALTERNANS

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Experimental studies have shown that ionic mechanisms of T wave alternans are dependent of the cellular metabolism of calcium.

**Method and results**: In 20 post acute myocardial infarction (AMI) patients, microvolt T wave alternans (MTWA) annalysis was done before and after intravenous administration of Diltiazem and Verapamil, during a standardized right atrial pacing protocol.

30 minutes after administration of Diltiazem the magnitude of MTWA was, compared to baseline: decreased in 50% of patients, increased in 30%, unchanged in 20% of cases. After verapamil the results were: decrease in 60%, increase in 20%, no change in 20% patients.

**Conclusion**: Administration of calcium channel blockers influence the magnitude of MTWA in the majority of patients. For the clinical practice, it is probably better, to temporary withhold administration of calcium blockers before MTWA testing.

## HEART RATE VARIABILITY AND PHYSICAL PERFORMANCE CHANGES INDUCED BY BIVENTRICULAR PACING IN CONGESTIV

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Cardiac resynchronization therapy (CRT) is a well-accepted therapy in patients with advanced, congestive heart failure (HF). In these patients, changes of mean heart rate (HR), heart rate variability (HRV) and physical performance after starting CRT have not been fully investigated. In this study we rewieved data stored on a CRT-D (Contak-Renewal II, Guidant, USA) implanted in 24 pts (mean age 60.6±3.8 years, QRS duration 149.6 ±6.8 msec, LVEF 19±0.9%) with symptomatic CHF (functional NYHA class >II) despite optimal pharmacological treatment. Sexteen pts have had ischemic dilated cardiomyopathy. Over a period of 16 weeks, weekly changes of minimum HR and mean HR, standard deviation of mean R-R intervals (SDANN) and degree of physical activity done by each patient, measured by

#### SUDDEN DEATH RISK STRATIFICATION

Activity Log Index (AL) of the device, were analysed. Moreover, a cardiopulmonary exercise testing was performed before and 4 months after implantation.

**Results**: after 16 weeks, CRT-D determined a significant decrease of minimum and mean HR (66.2  $\pm 16$  vs  $58.5 \pm 2.1$ , and  $78.6 \pm 18.2$  vs  $72.2 \pm 2.8$  bpm, respectively, p<0.04) and a marked increase of SDANN (63.5  $\pm 29.4$  vs  $88.4 \pm 19$  msec, p<0.004). Moreover, after 4 months of continuous pacing, a significant increase of physical performance, measured by AL (from  $4.3 \pm 1.9$  to  $11.2 \pm 2.6$  %units, (p<0.001) and by VO2 max (from  $12.6 \pm 1.3$  to  $17.4 \pm 1.7$  ml\kg\min, p<0.002) was observed.

**Conclusions**: in pts with advanced CHF, CRT provides a marked reduction of sympathetic delivery with a gradual increase of parasympathetic activity; these autonomic tone changes appear to be joined to a marked increase of physical performance. Favourable changes of HRV behaviour and of working performance may suggest a better mid-term prognosis in CHF pts.

## HEART RATE TURBULENCE: AN USEFUL NON INVASIVE RISK PREDICTOR IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE 1

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Background. Myotonic Dystrophy type 1 (DM1) is a multisystemic disease with an impairement of cardiac conduction system and lifethreatening tachyarrhythmias. Heart rate turbulence (HRT) was introduced as a non invasive tool for risk stratification. Aim of our study is to assess: HRT parameters in DM1 patients (pts) and in pts with frequent ventricular arrhythmias and structurally normal heart (VANH), and the correlation between HRT parameters and sustained ventricular arrhythmias (SVA) induced at electrophysiological study (EPS) in DM1 pts.

**Methods**. We performed HRT analysis, by a 24 hours ECG recording, in 15 DM1 pts (mean age 52±10 years) and in 15 VANH pts (mean age 54±9 years). We calculated the turbulence onset (TO), a percentage difference between the mean of first two RR intervals after a premature ventricular contraction (PVC) and the last two RR intervals before a PVC, and the turbulence slope (TS), a maximum positive slope of a regression line assessed over any 5 consecutive RR intervals within the 20 sinus RR intervals after a PVC. EPS was performed in all DM1 pts to evaluate the inducibility of SVA.

**Results**. No differences were observed in TS parameters between DM1 pts and VANH pts ( $12.3\pm4.2$  and  $9.2\pm3.9$  ms/RR, respectively), while TO values were significantly different between DM1 pts and VANH pts ( $-0.44\pm2.1$  and  $-2.91\pm1.8\%$  respectively; p 0.02). At EPS, a SVA was induced in 6 (40%) DM1 pts. TO values were  $-2.29\pm1.5\%$  in no inducible and  $2.32\pm1.3\%$  in inducible DM1 pts (p 0.008).

Conclusions. Our data suggest a dysfunction of the nervous autonomic system, assessed by HRT analysis, in DM1 pts respect to VANH pts. The difference is more evident in inducible DM1 pts that showed the most pathological TO values (>0%). Therefore TO seems an useful non invasive risk predictor of SVA induced at EPS in DM1 pts.

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### A NEW IMPLANTING TECHNIQUE THROUGH CEPHALIC VEIN

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Despite the large use of subclavian vein puncture for implantation of permanent pacemaker leads, direct venous cutdown remains a preferable technique. Aim of this study was to evaluate the feasibility and safety of a new technique for pacemaker implantation through the cephalic vein.

Methods. The vein was isolated, the distal end tied, and proximal hemostatic control attained. A 16-gauge thin-walled needle was gently inserted into the vein and fully advanced. A standard J wire was then advanced under fluoroscopy guidance to the subclavian vein. If the wire met no resistance, the appropriate-size dilator and sheath combination of a peel-away system was slipped over the wire. In case of dual chamber pacemakers we inserted two wires: the choice of the appropriate size depended on the diameter of the catheters to handle.

Results. All patients were implanted with tined bipolar atrial and ventricular leads. In 41 implants (mean age 75±34) performed with this technique and with the same operator the success rate was 28/41 (68,29%). Twenty patients received a dual chamber pacemaker and 8 patients a single chamber pacemaker. Globally 48 leads were successfully implanted. In the remaining 13 cases the attempts failed, but the cephalic vein reported no damages. In 2 patients we failed both the cephalic and the subclavian approaches. Only in 3 patients the cephalic vein was so thin to prevent any attempt for lead insertion. In case of dual chamber pacemaker, after the first lead implantation, it was always possible to insert also the second one. None patient reported any complication relating to the procedure. Conclusion. The described method is feasible in the majority of patients and it is safe in the overall patient population independently on the success of the first approach.

### INCIDENCE OF MUSCLE STIMULATION DURING VENTRICULAR AUTOCAPTURE THRESHOLD TEST

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With Autocapture the ventricular pacing threshold is automatically determinded and the output amplitude regulated to pace slightly above the threshold value. Every 8 hours or after loss of capture an automatic threshold search is started. During this test the pacemaker delivers a 4.5 V/0.5 ms backup pulse after every ineffective primary pacing pulse. The goal of this study was to evaluate the incidence of muscle stimulation caused by the 4.5 V backup pulse issued by Autocapture during the

threshold search algorithm.

**Method**: Autocapture threshold tests have been performed in 47 Patients (27 male) during routine follow up at least 4 weeks after implantation of a pacemaker Identity or Integrity (St. Jude Medical) that have a programmable Backup pulse. The configuration was randomized to unipolar or bipolar and the test performed in supine position, lying sideways and while sitting. After crossover of the backup pulse configuration the tests have been repeated.

**Results**: Muscle stimulation occurred in 2 Patients (4.3%) out of 47 in at least on position in unipolar configuration of the backup pulse. No muscle stimulation was observed with the bipolar backup pulse. Stimulation parameters were in the normal range: Threshold 1.0 +/-1.0 V; ER signal 12.1 +/-6.8 mV; Polarisation: 0.6 +/-0.4 mV.

**Conclusion**: In rare occasions a unipolar backup pulse of 4.5 V can cause muscle stimulation during Autocapture threshold test. Reprogramming the pulse configuration to bipolar solves this problem.

### THERAPY ADVISOR IN PACEMAKERS: C-STAR INTERIM RESULTS

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**Introduction**: Digital pacemakers have the ability to store a large amount of clinically relevant pacemaker and patient data. Analysis of this data in clinical practice may become very time-consuming and burdensome. In addition many pacemaker settings are left unchanged after implantation. Therefore an expert system, the Therapy Advisor (TA) (Vitatron C-series), was developed, which automatically analyses all data and indicates which diagnostics need attention. In addition it provides recommendations for optimizing the pacemaker therapy.

C-STAR evaluates this TA system.

**Methods**: Prospective, multicentre, observational registry. Inclusion: Class I/II pacing indication, Vitatron C60 DR/C50 D, Registry Consent Form. Interim analysis: 1st follow-up of 100 patients, changes in pacemaker settings and medication, following advices, evaluation of TA.

**Results**: 2-month follow-ups of 100 patients: 60% male, age: 72.6  $\pm$  10.2, indications: 47 SSS, 46 AV block, 4 drug induced bradycardia, 3 other.

Changes in pacemaker settings were mainly driven by the pacemaker diagnostics; drug therapy changes were equally driven by diagnostics and symptoms. 79% of the programming recommendations were followed. Main reason not to follow them was that it was not clinically necessary in the individual patient.

The most common message was: 'TA has nothing significant to report' indicating that no abnormalities were observed in the diagnostics

The questions 'Does the TA help assessing patients' and 'TA makes the follow-up more efficient' were evaluated by the investigator in more than 80% of the cases as neutral to positive.

**Conclusion**: The Therapy Advisor provides clinically relevant information for optimizing the pacemaker therapy and makes the follow-up more efficient.

### THE POSSIBLE INFUENCE OF THE RING (INDIFFERENT ELECTRODE) ON THE STIMULATION THRESHOLD

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Background: stimulation at the pacing threshold is dependent on the distance between the electrode(s) and the myocardial cells and the so called current density. The energy needed for anodal and cathodal stimulation is different and it was suggested that anodal stimulation from the proximal ring could play a role in the process of stimulation. Therefore we compared the measurements of pacing threshold (Thr) in uni- and bipolar, cathodal and anodal configurations in relation to unipolar anodal stimulation at the ring.

**Methods**: In 16 pts (9females/6males; age 73±12 yrs) with a pace-maker implantation 22 bipolar electrodes were tested for the stimulation Thr in the positions: bi- and unipolar cathodal (BiCath & UnCath) vs. bi- and unipolar anodal (BiAn & UnAn) and unipolar cathodal and anodal stimulation at the (indifferent) ring electrode. Thr was determined by decreasing the voltage in steps of 0,1 Volt until capture loss was seen and then by increasing in steps of 0,1 Volt till stable capture.

**Results**: The anodal stimulation Thr of the distal tip is always higher vs. the cathodal Thr: delta  $0.60\pm0.38$  Volt (bipolar, p = 0.0000003) or  $0.52\pm0.35$  Volt (unipolar, p = 0.0000008). The unipolar Thr is always lower (or at least equal at very low values) then the bipolar Thr: delta cathodal  $0.09\pm0.11$  Volt (p < 0.002), and delta anodal  $0.16\pm0.10$  Volt (p = 0.000003). The unipolar ring Thr was always high or very high vs

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cathodal bipolar Thr (configuration using the ring electrode) factor 2,8 till 33; average  $14\pm12$  (n= 8, p < 0,005).

**Conclusion**: the contribution of anodal stimulation at the proximal ring electrode to the effective stimulation in the standard bipolar configuration is very unlikely, because anodal stimulation threshold is average 14-fold higher then cathodal threshold. The proximal ring electrode in the bipolar configuration serves as a real indifferent electrode

### FRACTAL CORRELATION PROPERTIES AND VENTRICULAR PREMATURE BEATS IN CHAGAS DISEASE

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Chagas disease affects nearly 20 million persons in Latin America and is characterized by heart failure, ventricular arrhythmias, sudden death, and autonomic dysfunction. Detrended fluctuation analysis (DFA) is a nonlinear method of analysis of the HRV and three indices are obtained: alpha (global fractal correlation index), alpha 1 (short term), alpha 2 (long term). Unedited alpha 1 index was the best predictor of mortality in prospectives studies. The relationship among short-term HRV indices and ventricular ectopies is a matter of debate.

In order to study this relationship, we performed DFA in edited and unedited (with ventricular ectopic beats, VPC) series of RR intervals from Holter monitoring of healthy controls (group 0, n=27) and Chagas disease patients with normal ejection fraction (group 1, n=137) and with reduced ejection fraction (group 2, n=23). Patients were submitted to a standardized protocol including echocardiography and 24h Holter monitoring.

There was an inverse correlation (r=-0.63, p < 0,01) among the number of VPCs and alpha 1 index of short-term correlation. Unedited Alpha 1 index mean values were reduced only in Chagas disease group 2 (those with ventricular dysfunction). Both Chagas disease groups had altered edited DFA indices that were not detected by long-term time-domain analysis.

Abnormal edited DFA indices in both groups of Chagas disease patients suggest early vagal dysfunction. Unedited Alpha 1 value reduction was related to ventricular dysfunction and was largely influenced by the presence of VPCs, indicating a more random behavior of RR interval dynamics. The ability of these indices in stratifying the risk of sudden death in Chagas disease remains to be determined.

### IMPACT OF THE FULLY DIGITAL PACEMAKERS ON THE DAILY FOLLOW-UP ACTIVITIES

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The pacemakers (PMs) based on fully digital technology may not only improve the research activities but also the daily management of patients (Pts) during a standard follow-up (FU). The most important features helping the physicians in this context are the extremely high speed of telemetry, the high resolution EGM (800 Hz) and the automatic analysis of the stored diagnostic information to speed-up the decisional process during each FU (Therapy Advisor - TA). Aim of the study is to collect data about the time devoted to the FU of such a devices.

**Methods**. Patients (Pts) with indication for permanent DDDR pacing and implanted with C-60 Vitatron PM were followed-up at 1 (FU1) and 3 months (FU2) after implantation. During FU1 we performed the complete telemetry, the EGM analysis, the TA consultation, the analysis of pacing and sensing parameters and the final program-

ming of the device. During FU2 we only performed the telemetry, the EGM analysis and the TA consultation: reprogramming of the device was performed only in case of suspected malfunctions or indicated by the TA. Results. Till now 35 Pts were enrolled. At FU1 34 Pts ended the technical FU in 3′20″  $\pm$  41″. In 22 Pts (63%) the TA suggested the activation of a specific algorithm to reduce ventricular pacing: they were Pts with preserved AV conduction or paroxysmal AV block. The output setting was adjusted in all patients. One patient needed further investigation (8 minutes) for suspected atrial oversensing as suggested by the TA: atrial blanking was reprogrammed at 175 ms. At FU2 the mean time of FU was 3′05″  $\pm$  21″ without any need of further tailoring of the therapies. Conclusion. The TA, based on the high quality sensing combined with a very fast telemetry, represents an important improvement for standard management of implanted Pts.

#### CARDIAC RESYNCHRONIZATION THERAPY FOLLOW-UP

## PREDICTORS OF LONG-TERM SURVIVAL IN PATIENTS TREATED WITH CARDIAC RESYNCHRONIZATION THERAPY: THE INSYNC/INSYNCICD ITALIAN REGISTRIES

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**Introduction**: In patients with primary or secondary dilated cardiomyopathy and intraventricular conduction delays, Cardiac Resynchronization Therapy (CRT) was shown to reduce mortality at 12 months follow-up, when combined with an implantable defibrillator (ICD). We reviewed mortality data of patients enrolled in the In-Sync/InSyncICD Italian Registries to identify prognostic factors of mortality in patients treated with CRT.

**Methods**: The survival rate was evaluated for 317 patients  $(66\pm10 \text{years}, 262 \text{male}, 41\% \text{ ischemic}, \text{NYHA} 3.0\pm0.6, \text{QRS} 172\pm28 \text{ ms}, \text{EF} 28\pm10\%, 240 \text{ PMs}, 77 \text{ ICDs}), implanted before 2002 (median follow-up 36 months, IQR=28-44). The primary end point was death from any cause, the secondary end points were sudden and non-sudden cardiac death.$ 

Results: In our population there were 83 deaths (24 sudden, 36 non-sudden). All-cause mortality rate was 10.1 per 100 pts/year (95%CI, 7.0%-14.0%). Cardiac mortality rate was 7.3 per 100 pts/year (95%CI, 4.7%-10.7%): sudden cardiac mortality rate was 2.9 per 100 pts/year (95%CI, 1.9%-4.4%) and non-sudden cardiac mortality rate was 4.4 per 100 pts/year (95%CI, 3.1%-6.0%). Following baseline variables resulted independent prognostic factors of all-cause mortality at multivariate analysis: ischemic etiology (OR:2.0; 95%CI 1.1-3.7; p=0.021), NYHA Class IV (OR:4.7;95%CI 1.7-13.2;p=0.003), EF<=25% (OR: 2.0;95% CI 1.1-3.7; p=0.025). Considering the secondary end points, EF<=25% (OR: 3.1; 95% CI 1.0-9.2; p=0.042) resulted the only independent prognostic factor of sudden cardiac death, whereas ischemic etiology (OR: 3.7; 95% CI 1.6-8.6; p=0.002) and NYHA Class IV (OR: 12.6; 95% CI 2.6-60.7; p=0.002) were prognostic factors of non-sudden cardiac death.

**Conclusion**: These data confirm the negative prognostic value of ischemic etiology and seem to suggest the use of CRT in early stages of disease, before the patient become severely symptomatic (NYHA Class IV). The depressed EF represents the strongest factor for identifying patients eligible for ICD support.

## CARDIAC OUTPUT IN SEQUENTIAL BIVENTRICULAR PACING WITH SINUS RHYTHM IN HEART FAILURE PATIENTS

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Atrioventricular (AV) delay is an important parameter for the hemodynamic improvement of simultaneous biventricular (BV) pacing in heart failure (HF) patients. We analysed sequential BV pacing during optimal AV delay with cardioscreen impedance cardiography (Medis, Ilmenau, Germany) in HF patients with sinus rhythm (SR). Eight HF patients (age 66 +/- 12 years; 8 males; heart rate 67 +/- 9 bpm) with NYHA 2.8 +/- 0.4, LV ejection fraction 22 +/- 7% and QRS duration 162 +/- 32 ms were tested using transoesophageal left ventricular (LV) pacing and arterial pulse pressure (PP). In 7 responders, PP was higher during transoesophageal LV pacing than PP during spontaneous rhythm (90 +/- 28 versus 77 +/- 21 mmHg, P=0.015). Hemodynamic optimal AV delay after atrial sense was 112 +/- 12ms (n=8). In 5 responders, cardiac output increased from 3 +/- 1.4 l/min during simultaneous BV pacing to 3.6 +/- 1.6 l/min during sequential BV pacing (P=0.027) with 28 +/- 12 ms LV before right ventricular

(RV) pacing and optimal AV delay. Simultaneous BV pacing with optimal AV delay was optimal in 2 responders with 5.2 +/- 1.7 l/min cardiac output. NYHA class of the responder improved from 2.8 +/- 0.4 to 1.9 +/- 0.4 during 8 +/- 6 months BV pacing follow up (P=0.01). NYHA class 3 of the nonresponder not improved during hemodynamic optimal sequential BV pacing with LV 20 ms before RV pacing. In conclusion, sequential BV pacing with LV before RV pacing is able to improve cardiac output in HF patients with SR. Transoesophageal LV pacing may detect responders to BV pacing.

### CARDIAC RESYNCHRONIZATION THERAPY IN NYHA II PATIENTS: THE INSYNC/INSYNC ICD ITALIAN REGISTRIES

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**Introduction**: Cardiac Resynchronization Therapy (CRT) is currently being targeted to moderately and severely symptomatic heart failure patients (NYHA Class III and IV), with systolic dysfunction (Ejection fraction <=35%) and evidences of ventricular dyssynchrony (QRS >130ms)

Aim of the study was to assess the effects of CRT in mildly symptomatic patients (NYHA Class II) with respect to patients with standard indications.

**Methods**: 1232 patients ( $68\pm9$  years, 1010 male, 569 ischemic) were enrolled in the InSync/InSync ICD Italian Registries and followed for  $16\pm14$  months.

At baseline, 235 patients were classified in NYHA Class II (65 $\pm$ 10 years, 1.7 $\pm$ 1.0 hospitalizations for heart failure in the 12 months preceding the implant with a mean number of 9.3 $\pm$ 7.8 days of hospitalization), the remaining 997 were in NYHA Class III or IV (68 $\pm$ 9\* years, 2.3 $\pm$ 1.4\* hospitalizations with 22.2 $\pm$ 17.1\* days of hospitalization).

\*: p<0.001 versus NYHA Class II.

**Results**: In NYHA III or IV patients, we observed significant improvement of NYHA Class (from  $3.2\pm0.4$  to  $2.2\pm0.7$ #), ejection fraction (from  $27\pm10\%$  to  $34\pm12\%$ #), QRS width (from  $167\pm30$ ms to  $133\pm26$ ms#), mitral regurgitation degree (from  $2.2\pm1.0$  to  $1.8\pm0.9$ #). A reverse remodeling was apparent in this group with a reduction of LVEDD (from  $69\pm9$ mm to  $66\pm13$ mm#) and LVESD (from  $59\pm11$  to  $53\pm13$ #).

Patients classified in NYHA Class II at baseline improved in NYHA Class (from 2 to 1.9 $\pm$ 0.6#), ejection fraction (from 30 $\pm$ 10% to 36 $\pm$ 11%#) and QRS width (from 165 $\pm$ 31ms to 137 $\pm$ 27ms#), whereas other echocardiographic parameters did not appear significantly changed: mitral regurgitation degree (from 1.8 $\pm$ 0.9 to 1.7 $\pm$ 0.9). LVEDD (from 69 $\pm$ 10mm to 67 $\pm$ 12mm) and LVESD (from 57 $\pm$ 13 to 55 $\pm$ 14).

#: p<0.01, versus Baseline.

In both groups, 15% of patients required to be hospitalized for worsening of heart failure during follow-up.

Conclusion: Although ventricular reverse remodeling observed in sicker patients appears not significant in subjects with mild symptoms of heart failure, in these patients CRT results in significant improvement of functional status and cardiac function.

## IS THERE A DIFFERENCE BETWEEN PACING SITES IN CARDIAC RESYNCHRONIZTION TEHRAPY WITH RESPECT TO THE HEMODYNAMIC RESPONSE?

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INTRODUCTION: CRT is accepted to be a valuable tool in the treat-

#### CARDIAC RESYNCHRONIZATION THERAPY FOLLOW-UP

ment of patients with advanged heart failure and prolonged QRS duration. However, the optimal pacing configuration of multi site stimulation is not well established

METHOD: In 75 patients with heart failure class III-IV and QRS> 120 msec and a mean age of 67 + 10 years was studied. Temporary pacing leads (Biotronik TC 116) were placed in the RV apex (RVAP) and RV outflow tract (RVOT). Electrically isolated guidewires were positioned anterior (LVA) and posterior (LVPL) in the coronary sinus permitting unipolar stimulation. Pacing was performed in 5 different configuration: RVOT-RVAP, RVAP-LVPL, RVOT-LVPL, RVAP-LVA and RVOT-LVA in a VDD mode. Cardiac index (CI) was determined using echo Doppler flow measurements over the aortic valve, and the hemodynamic respons was determined by a relative increase in CI. For each patient the optimal site aswell as the second and third best were calculated.

RESULTS: The mean CI at baseline was 1,66 + 0,43 The hemaodynamic measurements of the optimal, the scond best and the third best site are summarized in the table (p-value <0,0001 for each site).

Site	CI	delta CI (%)	
Optimal Site	1,94 + 0,48	17,6 + 9,1	
Second best	1,90 + 0,47	15,1 + 9,1	
Third best	1,86 + 0,46	13,0 + 8,6	

**CONCLUSION**: The optimal site is significantly better than the second best site, so it is worth while to dtermine which site this is for the individual patient.

### UPGRADE TO BIVENTRICULAR PACING: THE INSYNC/INSYNC ICD ITALIAN REGISTRIES

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**Introduction**: Due to ventricular dyssynchrony induced by right ventricular pacing, heart failure (HF) patients (pts) with reduced ejection fraction (EF) implanted for antibradycardia indications may benefit by Cardiac Resynchronization Therapy (CRT).

**Aim**: To evaluate the outcome of pts undergoing device upgrade to CRT with respect to pts receiving a new implant for CRT.

**Methods**: 1232 pts (68±9 years, 1010 male, 569 ischemic) enrolled in the InSync/InSync ICD Italian Registries were followed for 16±14 months.

At the time of the implant, 243 pts were already paced for antibradycardia indications (Upgrade), the remaining 989 received a new implant for CRT (New Implant).

Results: In both groups we observed significant improvement of NYHA Class (Upgrade: from  $3.1\pm0.6$  to  $2.2\pm0.6$ #; New Implant: from  $2.9\pm0.6$  to  $2.2\pm0.7$ #), EF (Upgrade: from  $27\pm9$ % to  $35\pm11$ %#; New Implant: from  $27\pm10$ % to  $35\pm12$ %#), QRS width (Upgrade: from  $173\pm38$ ms to  $137\pm26$ ms#; New implant: from  $165\pm29$ ms to  $133\pm27$ ms#), mitral regurgitation degree (Upgrade: from  $2.2\pm0.9$  to  $1.8\pm0.8$ #; New Implant:  $2.1\pm1.0$  to  $1.8\pm0.9$ #), LVEDD (Upgrade: from  $68\pm9$ mm to  $66\pm12$ mm#) and LVESD (Upgrade: from  $58\pm10$ mm to  $53\pm12$ mm#; New Implant: from  $59\pm11$ mm to  $54\pm13$ mm#).

#: p<0.05 vs Baseline.

71% of Upgrade pts and 67% of New Implant pts (p=0.203) resulted clinically responder to the CRT (improved NYHA Class and no HF hospitalization).

Among Upgrade pts, the response to CRT was similar in healthier (NYHA Class II: 30 pts) and sicker pts (NYHA Class III and IV: 213 pts): 60% of NYHA II and 73% of NYHA III and IV pts resulted clinically responder (p=0.148), the relative increase of EF was  $28\pm33\%$  in NYHA II vs  $38\pm55\%$  in NYHA III and IV (p=0.557).

**Conclusion**: CRT induces clinical benefits also in pts with previous pacing device. In this group, the benefits are evident also in healthier pts, suggesting the use of CRT in subjects requiring the substitution of device even if less symptomatic.

### BENEFITS OF CRT IN CHRONICALLY PACED PATIENTS WITH HEART FAILURE: SHOULD WE UPGRADE?

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Background: Crdiac re-synchronization therapy (CRT) is becoming a mainstay of treatment for patients with drug-refractory systolic heart failure and intra-ventricular conduction delays. It was suggested that patients with wide QRS due to right ventricular pacing may benefit from CRT. This study was aimed to compare the benefit from CRT in patients with and without previous right ventricular pacing. Methods: A total of 59 patients with CRT were studied. They were divided into two groups. Group A (n=17) included patients that had right ventricular pacing before CRT implantation. Group B (n=42) patients had no pacing prior to CRT implantation. Response to CRT was assessed using clinical (New York Heart Associtation class, 6 minute walk test) and echocardiographic measures (Left ventricular dimesions and ejection fraction, mitral regurgitation grade)

Results: The mean follow up period was 4.9±1.46 months. There were no significant difference at baseline between groups, other than a wider QRS in Group A patients (205±46 vs. 166±35, p=0.0002). At the end of follow up NYHA functional class improved by 0.79 points on average in Group A patients, compared to 0.23 points in Group B patients (p=0.002), there was no significant difference between groups with regard to changes in LVDD, LVSD, LVEF, 6 minute walk distance, or MR grade.

**Conclusions**: Patients with right ventricular pacing and refractory heart failure had a significant clinical improvement with CRT, which was even more prominent than that gained by patients without a previous pacemaker, and should be considered for upgrading to CRT.

#### TAILORING PERMANENT CARDIAC PACING

## WHICH IS THE RELATION BETWEEN ATRIAL FIBRILLATION DURATION AND PHISICALLY DISABLING SYMPTOMS IN PM PATIENTS?

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**BACKGROUND**. One of the controversial strategies to diagnose and treat timely atrial fibrillation (AF) in pacemakers (PM), is the persistence of physically disabling symptoms which alert the patient at home of a possible episode recurrence.

**AIM**: in dual chamber PM, identify which is the range for AF duration which have the most disabling effect on patient physical activity and symptoms.

METHODS. 211 pacemaker (PM) follow ups from 111 patients were considered (INSIGNIA, Guidant). Mean AF episode duration (AF-D) was analyzed from PM diagnostics and used to divide data in the following subgroups: no AF or inferior to 1 minute (O), 1 minute to 1 hour (M), 1 hour to 1 day (H), 1 day and more (D). Differences were looked in these groups for the following variables: mean % of daily activity during the follow up period (%ACT), maximum decrease in daily activity with respect to mean value (M-%ACT) and physical function score (PF). %ACT and M-ACT were retrieved from ACTIV-ITY LOG, a daily register of patient physical activity.

**RESULTS.** Distribution of AF episodes were: O:58%; M:31%; H:6%; D:5%. A trend in decrease of %ACT was found with increasing AF-D (O:  $6.1\%\pm2.6$ ; M:  $5.8\%\pm2.4$ ; H:  $4.7\%\pm1.2$ ; D:  $4.3\%\pm1.8$ : F=246; p<0.01), strong decrease in M-%ACT was particularly relevant in the D group (O:  $-32\%\pm15$ ; M:  $-38\%\pm37$ ; H:  $-44\%\pm26$ ; D: %  $-85\%\pm10$ ; F=56; p<0.01). No clinically relevant difference were found in PF (O:  $0.77\%\pm0.19$ ; M:  $0.71\%\pm0.18$ ; H:  $0.76\%\pm0.06$ ; D:  $0.84\%\pm0.1$ ; p=NS)

**CONCLUSION**. Despite high incidence of paroxysmal AF in pm patients, only few perceive relevant symptoms leading to abrupt decrease of daily physical activity, being these in particular patients with single AF episodes lasting in the range of 24 hours. Frequent PM follow ups are suggested to diagnose timely AF rather than rely on patient symptoms.

## PHYSIOLOGICAL RATE ADAPTATION WITH AN ELEVATED BASIC RATE FOR PREVENTION OF PAROXYSMAL AND PERSISTENT ATRIAL FIBRILLATION

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Atrial overdrive pacing may suppress atrial extrasystoles and thus prevent the onset of atrial fibrillation (AF). However, after restoration of the sinus rhythm the atrium is the most vulnerable to reinitiation of AF. The aim of our study was to evaluate the efficacy of rateadaptive pacing based on myocardial contractility (DDD-CLS), used in combination with an elevated basic rate, in diminishing AF in patients with Brady tachycardia syndrome. Twenty-six patients with a mean age of 59 ± 10 years (57% male, 65% presenting Chagas disease) were enrolled in a prospective study. Each patient was taking amiodarone (400 mg/day) during the study. Two months after implantation the patients were randomized to receive either DDD pacing at a basic rate of 60 bpm or DDD-CLS pacing with a basic rate set to 80 bpm. Mode switching option was activated in all patients and pacemaker statistics were used to count the number of mode switch episodes. A 3-channel 24-hour Holter ECG was obtained in all patients. The mode crossover was performed after 3 months. Holter ECG recordings revealed a significant reduction in the number of atrial extrasystoles (p < 0.01) and the number of ventricular complexes during AF (p < 0.05) in the DDD-CLS pacing with an elevated basic rate. The number of mode switch episodes recorded in the pacemaker memory over 3 months was also reduced during DDD- CLS pacing with an elevated basic rate (p < 0.001). In conclusion, myocardial-contractility based rate-adaptive pacing with a basic rate of 80 bpm reduced the incidence of paroxysmal AF.

### CLINICAL PROGRAMMING OF AV INTERVAL IN CARDIAC RESYNCHRONIZATION THERAPY

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Optimization of the left heart AV interval plays a critical role in the success of cardiac resynchronization therapy (CRT). An abnormal left heart AV interval may cause pacemaker syndrome due to truncation of atrial transport, and diminish or abolish the benefits of CRT. Since it has been shown that the interatrial electromechanical delay (IAEMD), the interval between the right heart P wave and the onset of the A wave of mitral flow, can be predicted from the width of the P wave of the surface ECG or the left atrial size, it was hypothesized that clinical predictors of above delay may allow programming the AV interval. Therefore, a simple algorithm is presented and demonstrated by a computer simulation of the hemodynamic consequences of AV interval programming. With this method it would be possible to program the pacemaker with three increasing levels of precision, depending on the availability of clinical information: a) level 1, where the AV interval is programmed using only a clinical judgment of the left atrial size; level 2, where the AV is programmed by measuring the P wave duration by surface ECG and/or the left atrial dimension by M-mode echocardiography, and level 3, where the actual value of IAEMD (derived from echo-Doppler) is input. The algorithm automatically adjusts the AV interval for the P-sense offset, atrial sensing or atrial pacing, and V-V delay, which results in a normal left heart AV, beat-by-beat, independently from rate and/or pacing mode.

## EFFECTIVENESS, SAFETY AND REDUCTION OF THE TIME OF VENTRICULAR FIBRILLATION INDUCTION WITH DCFIBBER METHOD

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**PURPOSE**: the most critical phase during Implantable Cardioverter Defibrillator (ICD) implantation is Ventricular Fibrillation (VF) induction and device testing.

Traditional methods of  $\overline{VF}$  induction include use of incremental ventricular pacing (burst or ramp), alternate current or delivering a shock on T wave (SoT). These methods, while effective in the vast majority of patients, suffer significant drawbacks.

In St. Jude Medical ICDs a new method of VF induction named DC-fibber is available. It consists in delivering a 9 Volt Direct Current (DC) pulse between defibrillation coils and the can of the device. The only parameter that is necessary to program is the pulse duration (from 0,5s to 5s, in 0,5s steps).

Several studies demonstrated the effectiveness and safety of DC-fibber with duration greater or equal to 2s, especially compared to SoT method.

The aim of the study is to evaluate if it is possible to reduce, further on, the time of VF induction with DC-fibber method without losing effectiveness and safety.

MATERIALS AND METHODS: 31 patients (22 males) with a mean age of 65±10 years were evaluated. Underlying etiology was Dilated Cardio-Myopathy in 52%, Coronary Artery Disease in 42%, idiopathic in 6%. Left Ventricular Ejection Fraction was 32±10%. NYHA class was 2,4±0,7. Antiarrhythmic drugs (AAD) taken at the time of ICD implantation were amiodarone and beta-blokers in 19% of the pa-

#### TAILORING PERMANENT CARDIAC PACING

tients, amiodarone in 61%, sotalol in 6%, no AAD in 14%.

Patients were implanted with single (n=12), dual (n=12) and triple chambers (n=7) devices.

At least one sustained VF was induced in all patients: in 23 cases it was done with DC-fibber at 0,5s, in 1 case with DC-fibber at 1s, in 4 cases with DC-fibber at 2s, in 1 case with SoT, in 2 case with Non Invasive Programmed Stimulation.

RESULTS: VF induction was successful in all the patients at first attempt, except for 1 case in whom DC-fibber at 0,5s was not successful and was necessary DC-fibber at 1s successful at first attempt. CONCLUSIONS: It is possible to reduce substantially the DC-fibber duration, saving energy and without losing effectiveness and safety. The optimization of the duration of the DC-fibber pulse can be useful for reducing the time of induction and anesthesia and the possible risks in patients implanted with ICD.

#### PACEMAKER POCKET PAIN: A MAMMALIAN SOLUTION

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PURPOSE: Painful pacemaker pockets can be very disabling for patients and frustrating for surgeons to treat. Solutions to date include repositioning beneath the pectoralis muscle, injections of steroids, lipoinjection and implantation of pacemaker by femoral vein. Originally placed in the retro-mammary position for cosmesis, this location also proved very effective for intractable pacemaker pocket pain. MATERIALS AND METHODS: Seventeen patients: 7 young women (Avg. age 26 yrs) and 10 children (Avg age: 14 years) underwent DDD pacemaker insertion (except one AAI) for complete heart block (5) neurogenic sycope (7), long Q-T syndrome (2) or other (3). In fourteen patients, the retro-mammary location was chosen for either cosmetic (11) or sports (3) reasons. Three patients had re-location of the generator specifically for painful pocket site. This surgery involves first a one inch subclavicular incision to place the endovascular leads via the subclavian vein, tunneling of the leads to a vertical anterior axillary line incision and fashioning a pocket anterior to this line behind the left or right breast.

**RESULTS**: All 17 Patients are asymptomatic from their pacemakers at a mean followup of 4 years 3 months. One patient had to have one lead repositioned early postoperatively (one of 33 leads: 3% lead dislodgement rate). Two patients have returned for generator replacement without incident. No infections have occurred. And furthermore monitoring remains unimpaired.

**CONCLUSIONS**: Retro-mammary placement of pacemaker generators is not only cosmetic in young women and girls, but offers a solution for chronic pacemaker pocket pain and possibly even for pacemaker twiddlers.

## THE USE OF FIBRILLAR REGENERATED OXIDIZED CELLULOSE (SURGICEL FIBRILLAR - JOHNSON & JOHNSON) TO PREVENT BLEEDINGS IN CARDIOLOGY

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**Introduction**: During the last years there has been a remarkable increase of pacemaker devices and ICD (implantable defibrillator). Moreover, a lot of patients who have to undergo a device implantation take anti-platelet and/or anti-coagulant drugs that are not easy to manage.

Survey: From May to June 2003 we selected 30 patients who took

anti-platelet and anti-coagulant drugs who needed pacemaker or ICD devices or replacement of medical devices. Of the 30 selected patients, 19 took anti-platelet products for coronary and/or arterio-sclerotic peripheral vascular pathology, 11 took anti-coagulants for atrial fibrillation or with mechanical cardiac valvular prosthesis. 4 among the patients with anti-coagulant therapy took Coumadin.

In some cases the surgery has been carried out under the effect of the above mentioned drugs and, therefore, with potential risk of bleedings during and after the operation. This was due to clinical problems (mechanical cardiac valvular prosthesis or the presence of AV syncopal arrest impossible to control with drugs in time) or to managing problems (Day Hospital of old people who had forgotten to take the drugs).

The surgery ended with the covering of the surgical pouch with fibrillar regenerated oxidized cellulose (Surgicel Fibrillar-Johnson&Johnson).

Within one week after the surgery all patients restarted their antiplatelet and anti-coagulant pharmacological therapy. An outpatient follow-up visit was scheduled 7-10 days later in order to check the wound

Results: None of the patients had important hematomas complications during the post-surgical course nor a decrease of the hematocrit values. Only 2 patients with mechanical cardiac valvular prosthesis with oral anticoagulant therapy who had undergone emergency surgeries had a small hematoma, without decrease of hematocrit value and without any complications.

Conclusion: The use of fibrillar regenerated oxidized cellulose (Surgicel Fibrillar-Johnson&Johnson) once the pacemaker and ICD devices had been implanted in heart patients in anti-platelet and anticoagulant pharmacological therapy considerably reduces the risk of bleedings during and after the surgery, releasing also a potential antibacterial effect.

#### RIGHT ATRIUM ABLATION

# RIGHT ATRIAL RADIOFREQUENCY COMPARTIMENTALIZATION IN PATIENTS WITH ATRIAL FIBRILLATION. LEFT ATRIAL EFFECTS BY ELECTROANATOMIC CARTO EVALUATION

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Atrial fibrillation (AF) radiofrequency ablation (RFA) target is present at the level of pulmonary vein ostia in the left atrial (LA). Our esperience refers about a previous casistic of patients (Pts) affected by persistence AF insensitive to pharmacological therapy (PT), treated with right atrial (RA) RFA compartimentalization (CO) underwent LA electroanatomic CARTOXP evaluation.

Material and Method: 45 Pts affected by persistence AF insensitive to pharmacological therapy, treated with RA RFA CO after electrical cardioversion. The RFA was performed, using electroanatomic CARTOXP mapping, with a septal line superior vena cava - inferior vena cava and cavotricuspid istmus block, by means 8 mm tip ablating catheter. Among them 20 Pts refers after 3±10 month, during PT, symptomatic parossistic AF. Then they were treated with transeptal approach on the LA target.

**Results**: The LA electroanatomic CARTOXP basal mapping demonstrated a significative atrial potential reduction at the atrial septal and at the right pulmonary vein ostia level on the posterior atrial wall, with vein disconnection from the sinus coronary pacing.

**Conclusion**: The RA CO may be useful to complete the atrial substrate modification to AF RFA.

## ROLE OF ELECTRO-ANATOMIC FEATURES OF CAVOTRICUSPIDAL ISTHMUS TO PREDICT OUTCOME IN ATRIAL FLUTTER

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Materials and methods: 168 patients (Pts) with typical atrial flutter (AFL) were treated by radiofrequency ablation (RFA) with CARTO system. On the basis of long term outcome, patients were divided into three groups: 1)stable sinus rhythm (SR) 2) new post-ablation atrial fibrillation (AF) 3) AFL recurrence. Electro-anatomical parameter were measured: 1) voltage at anterior, middle and posterior sector of the cavo-tricuspidal isthmus (CTI) (site a, b, c) 2)perpendicular and longitudinal conduction velocity 3) height of coronary sinus ostium (CSO) 4) depth of CTI 5)length of CTI 6)diameter of TVA.

Results: During the follow-up period (27.5 ± 14.4 months) 110 Pts maintained SR, 39 Pts showed new AF and 19 Pts AFL recurrence. At multivariate analysis, mean voltage, height of CSO, depth and length of CTI represent, all together, good predictors of maintenance of stable SR (pseudo-r2 64.6%), the voltage at sites a and b, and the depth and length of CTI represent, all together, relatively good predictors of new post-ablation AF (pseudo-r2 41.5%), while the height of CSO alone represents a good predictor of AFL recurrence (pseudo-r2 52.8%).

**Conclusions**: RFA of AFL performed by using the CARTO system shows, in the present study, a low incidence of AFL recurrence (5.3%)and of new post-ablation AF (22.3%), and a good relationship between electro-anatomical features of CTI and possible outcomes of the procedure.

### RANDOMIZED STUDY ON TWO DIFFERENT APPROACH FOR RF ABLATION OF TYPICAL ATRIAL FLUTTER

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Only few data exist on the importance of the site of lesion in success rate and in procedural time of RF ablation of typical atrial flutter. Since May 2004 to July 2004, 16 patients (13 male, mean age 59+3 yrs) underwent tricuspidal isthmus ablation in our Lab. Pts were randomized to receive a posterior or a posteroseptal lesion. If there still was isthmus conduction after 2 complete isthmus lesions, the procedure was considered unsuccessful and the patients received one or more RF pulses in the other site.

All the procedures were performed with an 8 mm tip ablation catheter

10 pts (8 male, mean age  $60\pm10$  yrs, group A) received a posterior lesion and 6 pts (5 male, mean age  $57\pm14$  yrs, group B) a posteroseptal approach.

The clinical characteristics of the two groups were comparable. All procedures but 2 were performed during pacing from the coro-

nary sinus in group A (in sinus rhythm) and all but 3 in group B. We did not find any differences in term of fluoroscopy time, RF total time and RF total pulses between the two groups. 3 pts in group A still had a conduction in the tricuspidal isthmus after 2 complete lesions whilst no pts from group B were switched to the other ablation site: this difference was not significant (p = 0.16).

The tricuspidal isthmus ablation is a very successful procedure for the treatment of typical atrial flutter. As demonstrated by another recently published experience, the site of ablation does not seem to be important in determining success rate and procedural duration.

#### COMPARATION OF TWO DIFFERENT APPROACHES DURING RADIOFREQUENCY ABLATION OF TYPICAL ATRIAL FLUTTER: A RETROSPECTIVE ANALYSIS

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BACKGROUND: Typical atrial flutter often results from a macroreentrant circuit bounded by specific anatomic structures within the right atrium. Radiofrequency (RF) ablation of the inferior vena cavatricuspid valve isthmus can interrupt the circuit. The aim of this study is to compare two different approaches to atrial flutter ablation.

METHODS: 20 patients (group A, 13 male and 7 female, age 65 +/-7) underwent typical atrial flutter ablation with a standard approach, 12 patients (group B, 4 male and 8 female, age 63 +/- 8) with a novel one. Both groups received RF isthmus ablation with a 8mm tip catheter inserted trough the right femoral vein.

For group A patients, the isthmus block was validated during coronary sinus pacing, observing the change in the right atrial activation registered by a 20-poles catheter, inserted by a femoral approach to map the tricuspid valve annulus.

For group B patients, a non fluoroscopic system for endocardial navigation (Localisa System-Medtronic) associated with a unusual catheter placement was used. The 20 poles catheter, inserted through the left subclavian vein, was used for right atrial mapping, with the distal electrodes into the coronary sinus (CS). By this configuration the clock-wise block was validated by a CS pacing, and the counterclock-wise block in sinus rhythm. The breaktrought was generally close to electodes n. 12-13. The electrodes close to the isthmus lesion registered a double activation signal.

**RESULTS**: The procedural time was 120 +/- 30 minutes (group A) vs

#### RIGHT ATRIUM ABLATION

90 +/- 15 minutes (group B). The fluoroscopy time was 50 +/- 10 minutes (group A) vs 15 +/- 5 minutes (group B). No difference was reported in number of RF applications, temperature and power (number of RF applications was 10+/-3, power 60+/-8 W, temperature 55+/-6 °C in both groups).

**CONCLUSION**: The novel approach is as effective as a standard one. The fluoroscopy time and the procedural time are lower if compared with a standard approach. Furthermore the use of only one catheter for mapping and atrial stimulation allowes an easy navigation with the mapping/ablation catheter.

#### RADIOFREQUENCY CATHETER ABLATION OF POSTERO-SEPTAL ACCESSORY PATHWAYS IN PAEDIATRIC AGE

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Purpose: Radiofrequency catheter ablation (RFCA) of the posteroseptal accessory pathways(AP) has been reported to be more difficult than for AP located in other areas. A high proportion of RFCA of postero-septal AP require ablation from coronary sinus(CS) or coronary veins. Aim of the study was to evaluate the efficacy and risks of RFCA of postero-septal AP in a single centre paediatric population. Methods: between January 2002-September 2004, 14pts (7M/5F,aged 8-17 years, mean age 13,08±2,8) with a postero-septal AP underwent attempt to RFCA. Results: In the 14pts with a postero-septal AP (9with overt ventricular pre-excitation, 5 with concealed by-pass tract) were delivered RF in the earliest site of activation on the mitral or tricuspidal annulus. Time of procedure, including anaesthesia induction, was 136±57min, time of radiation exposure was 49±20 min. Successful RF pulses were delivered on right postero-septal area in 4pts, on left postero-septal area in 2pts, in the proximal CS in 5pts. True epicardial postero-septal AP were found in 3pts and the RFCA was considered to be not feasible. Four weeks and 12weeks after RFCA all patients underwent a non-invasive clinical-instrumental evaluation. Only a patient underwent a second procedure for recurrence of arrhythmias. Conclusion: RFCA of postero-septal AP in paediatric age is technically challenging. More RF pulses, longer procedure time and longer radiation exposure are needed to achieve successful results, and recurrences of AP conduction are not unusual.

## USEFULNESS OF A NON FLUOROSCOPIC NAVIGATION SYSTEM DURING ECTOPIC ATRIAL TACHYCARDIA RF ABLATION

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RF ablation (RFA) of ectopic atrial tachycardia (EAT) is highly successful but a significant radiologic exposure is needed due to the 3D complex arrangement of the substrate.

Aim: It was to assess feasibility,accuracy and safety of EAT RFA,guided by a 3D non fluoroscopic navigation system (Localisa), which allows to display the real-time visualization of conventional catheters and a rapid delineation of the regional earliest isochrones. Methods: 24 pts with 25 EAT (20 female) underwent RFA (9 non-automatic; 3 non-paroxysmal; 2 tachy-cardiomyopathy): crista terminalis (10; 6sinoatrial), septum (8; 6parahissian), tricuspid annulus(5), superior vena cava(1), left side (1; left inferior pulmonary vein). An active fixation reference atrial lead was used. Sites of RFA were the earliest bipolar and unipolar activation (QS-type with fast intrinsec deflection). High density spatial resolution during mapping of the region with the earliest isochrones was obtained after positioning multipolar reference catheters near this region.

Results: RFA was effective and safe in all pts.During 15  $\pm$  7 m of

follow-up an early recurrence was observed (crista terminalis EAT) then suppressed with betablocker therapy (before ineffective). Mean fluoroscopic time for the active fixation of reference catheter and for the mapping and ablation procedure were 2.9±0.1 and 11.3±7 minutes respectively. In 6/15 pts (in 5/6 parahissian) RFA was effective during sinus rhythm after marking the sites with bumping or early interruption followed by abrupt displacement of the catheter tip.RFA was effective during sinus rhythm at sites overlapping the marked sites at the same tachycardia atrial pacing rate. In 4 EATs RFA was successful at sites with low voltage spikes preceding the intrinsic deflection of unipolar QS and the breakthrough of endocardial activation (QS-unipolar site). In 2 EAT the area of origin was wide (0.7-0.9 cm2).

Conclusion: Non-fluoroscopic intracardiac navigation system LocaLisa allows to perform with high accuracy and safety RFA of EAT minimizing the radiological exposure,namely in case of wide substrate(>0.5 cm2),susceptible of thermo-mechanical stunning or located in the atrioventricular nodo-hissian region.

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### BIFASIC EXTERNAL ELECTRICAL CARDIOVERSION IN PERSISTENT ATRIAL FIBRILLATION: THE EXPERIENCE OF A SINGLE CENTRE

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**BACKGROUND**: external electrical cardioversion for atrial fibrillation is the most common, safe, effective and cheap procedure for the restoration of sinus rhythm, in patients with persistent atrial fibrillation. The development of bifasic defibrillators allowed for higher success rates of conversion. However the best energy and its incremental steps are not yet identified on standards protocols.

**METHODS**: 98 patients (60 males and 38 females), mean age 66 years (DS 8), with persistent atrial fibrillation undergone to electrical cardioversion using a bifasic defibrillator with the electrodes placed in the anterior-lateral position. The starting shock energy was selected arbitrary by the executor doctor. Left atrial dimensions (anterior-posterior diameter) were measured by standard transtoracic echocardiography.

**RESULTS:** procedure was effective in the majority (92%), without significantly statistical difference between the average of atrial dimensions in the group with restoration of the sinus rhythm and in the group without this (44.5 mm vs 43.5 mm, p = 0.7).

The restoration of the sinus rhythm was obtained using a start energy lower or equal to 70 J in the 18.6% of the patients, using 100 J in the 93%, and 200 J in the 100%.

**CONCLUSIONS**: the effective of electrical external cardioversion in acute seems to be not correlated to the left atrial dimensions.

In our experience just a less number of patients recover sinus rhythm with a energy lower or equal to 70 J and the majority of restorations of sinus rhythm were obtained with higher starting energy, thus it is possible that a starting energy of 100 J is more effective against cumulatives energy starting by lower levels but with a total major erogation of energy.

An energy of  $100\,\mathrm{J}$  moreover causing less postprocedural pain and it is thus preferable to a higher value of  $200\,\mathrm{J}$ .

## FACILITATING CARDIOVERSION OF ATRIAL FIBRILLATION WITH IBUTILIDE PRETREATMENT AND TRANSTHORACIC BIPHASIC SHOCK

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Cardioversion of atrial fibrillation (AF) with standard monophasic transthoracic shock is significantly facilitated by combined pretreatment with ibutilide. No data are available about biphasic cardioversion and pretreatment with ibutilide. Aim of this study was to randomly and prospectively compare the efficacy of transthoracic biphasic cardioversion of AF with and without pretreatment with ibutilide.

Methods. Fifty consecutive patients, admitted in our institution for symptomatic persistent AF after failure of at least two attempts of pharmacological cardioversion, were enrolled and randomised in 2 groups: immediate cardioversion with biphasic shock (group 1) or pretreatment with ibutilide followed by cardioversion with biphasic shock (group 2). In group 2 patients, ibutilide was administered intravenously in 10 minutes through an infusion pump at a dose of 0.01 mg/kg. After the administration of ibutilide, a pause of 10 minutes was observed before the patients underwent biphasic cardioversion. Patients with the theoretical risk of ventricular arrhythmia due to ibutilide were excluded. Results. All patients in the two groups were successfully cardioverted (100%). The energy delivered and the number of shocks required for cardioversion were significantly lower in patients treated with ibutilide than in untreated patients. A relatively low shock energy was needed for cardioversion in the ma-

jority of patients in both groups: 11 out of 25 patients (44%) in group 1 were cardioverted at the first attempt with 50J. In group 2, 15 out of 23 patients (65%) were cardioverted at the first attempt with 50J. The number of patients cardioverted at the first attempt with 50J was significantly higher in group 2 than in group 1, as assessed by the c2 test: p=0.018. Conclusion. The energy requirement for transthoracic biphasic cardioversion of AF is lowered by pre-treatment with ibutilide. Biphasic shock is always effective and ibutilide administration is safe in a selected patient population.

### THE EFFECT OF PHARMACOTHERAPY ON THE RESULTS OF EXTERNAL CARDIOVERSION.

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Several studies had verified the data about the influence of angiotensin system on atrial remodulation, its relation with atrial fibrillation (AF) and frequency of early relapses after external cardioversion (ECV). Our aim was to analyse the effect of possible pharmacotherapy patterns on AF relapses after ECV.

**Method**. We compared 2 groups of pts with chronic AF (3 till 12 months), LA size 4.0 to 5.5 cm, anamnesis of AF at least 3 years, mean age 61.4 years.

Group I: 128 pts 2 weeks before ECV used amiodarone (AMIO) 200mg bid and angiotensin-converting-enzyme (ACE) inhibitors, group II used just AMIO in a similar pattern. Both groups just before ECV had IV 600 mg AMIO. The same was repeated also after ECV. We compared the data: rate of AF relapses after ECV during the first hour and 24 hours, 7 and 30 days, 3 un 6 months. We compared the effectiveness in groups where AF was shorter or longer than 6 months. Results. Gr. I had a lesser number of early relapses (first hour 7.6% vs 14.9%), during 24 hours 8.8% vs 18.5%; p<0.001. Number of relapses in distant period of time continued to increase: gr. II after 30 days 15.4% vs 28.6%, and in 6 month follow up persistent SR was in gr. I 73.4% vs 56.4%; p<0.02. Number of relapses was greater for patients with AF longer 6 months in both groups, but more in group II.

**Conclusions**. Duration of AF has an essential influence on the effect of cardioversion. ACEi, when combined with AMIO significantly affects the results of ECV and makes maintenance of SR more effective in distant period. Usage of AMIO pre and post EVC helps to avoid early relapses.

### ELEVATED LEVELS OF C REACTIVE PROTEIN PREDICT ATRIAL FIBRILLATION RECURRENCES

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**Background**. Previous studies have found a correlation between elevated levels of C-reactive protein (CRP) and presence of atrial fibrillation (AF). However, the relationship between CRP levels and risk of recurrence after cardioversion of persistent AF has not been previously investigated.

**Methods**. CRP levels were assessed at baseline in 102 consecutive patients who underwent successful electrical cardioversion for persistent AF lasting > 48 hours. All patients received antiarrhythmic therapy and clinical follow-up for recurrence of AF was performed up to 12 months.

**Results**. Patients were divided into two groups according to CRP levels. A total of 33 patients (65±11 years, 64% men) had low CRP levels (£2 mg/L, low CRP group), while 69 patients (67±11 years, 54% men) had high CRP levels (>2 mg/L, high CRP group). The two

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groups were similar for age, sex, hypertension (63% vs 73%), diabetes (9% vs 12%), ejection fraction (55 $\pm$ 15% vs 61 $\pm$ 12%), left atrial diameter (45 $\pm$ 6 vs 47 $\pm$ 5 mm) and duration of AF (85 $\pm$ 105 vs 88 $\pm$ 129 days, P=NS for all). Prevalence of new-onset AF was 22% in the high CRP and 24% in the low CRP group. Drug treatment was similar in the two groups, but the high CRP group had a more frequent use of amiodarone and a lower use of propafenone.

AF recurrence in the first 90 days after cardioversion was significantly higher in the high CRP vs. low CRP group (34% vs 9%, P=0.006). At 12-month follow-up there was still a trend towards higher recurrence rate of AF in the high CRP group (59% vs 39%, P=0.05).

**Conclusion**. Higher CRP levels are associated with higher rate of recurrence of AF after successful cardioversion. These results support the hypothesis that inflammatory markers may identify patients with higher risk of recurrence of AF.

## CLINICAL PREDICTION OF TIME TO RECURRENCE OF PERSISTENT ATRIAL FIBRILLATION AFTER CARDIOVERSION

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**Purpose**: To identify independent clinical predictors of time to first recurrence (TTFR) of atrial fibrillation (AF) after cardioversion to sinus rhythm.

Methods: Out of 335 patients with first persistent nonvalvular AF ever experienced, cardioversion was successful in 255 patients and they were assigned to further follow-up until the development of permanent AF or at least one year in continuous sinus rhythm. Baseline clinical and other parameters were recorded prior to cardioversion and each patient received a Class IC or III antiarrhythmic drug after successful cardioversion. Multiple logistic regression model within 95%CI was designed for identification of independent predictors of TTFR of AF.

**Results**: Patients were 17-78 years old (54 +/- 11.7) and AF lasted 48 hours to 72 months (8.6 +/- 13.5 months) before cardioversion, 101 patients were females, 124 (37.0%) had lone AF, arterial hypertension was present in 140 patients (41.8%), coronary heart disease in 25 (7.5%), cardiomyopathy in 39 (11.6%), heart failure in 33 patients (9.9%) and noncardiac disorders in 38 patients (11.3%). AF lasted more than 48 hours in 278 patients (83.0%) and longer than 1 year in 69 patients (17.9%). Follow-up was 0.5 to 15 years (4.4 +/- 3.2). Recurrent AF was documented in 215 patients (84.3%) with TTFR ranging from 2 weeks to 12 years (24.3 +/- 22.8 months). Statistic model with dependent variable TTFR and independent clinical variables mentioned above identified coronary heart disease (relative risk 3.0, p 0.004), heart failure (RR 1.8, p 0.031), AF >1 year (RR 3.9, p 0.002) and AF >48 hours (RR 2.4, p 0.012) as independent predictors of TTFR.

**Conclusion**: Patients with coronary heart disease, prior heart failure and/or long-lasting AF are at higher risk of earlier recurrence of AF than others. Such patients should be assigned to amiodarone or to frequency control strategy early in the course of treatment.

### CHANGING OF TEI-INDEX AFTER SUCCESSFUL CARDIOVERSION FROM CHRONIC ATRIAL FIBRILLATION

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**Background**: TEI index is relatively new index of combined systolic and diastolic myocardial performance, easily measured, reproducible and has a narrow range in normals. The purpose of this study was to compare the changes in TEI index according to different an-

tiarrhythmic drug therapy during the period of myocardial remodelling after successfull cardioversion (CV) from chronic atrial fibrillation (AF) and to compare it to the other diastolic parameters as well. **Method:** 153 patients(74 F, 79 M, mean age 61,9 y)with AF, after CV were devided in 3 groups according to drug treatment: 1:beta blocker (bisoprolol 5 mg, atenolol 50 mg, sotalol 160 mg/day)2: propafenone 450 mg/d,3: amiodarone 200 mg/d. The diastolic function and the TEI index were measured with pulsed Doppler 48 hours after CV and 3, and 6 months after, respectively. Following data were obtained: standard systolic and diastolic dimensions, EF, peak transmitral inflow velocities and their ratio (E/A), dec. time of the E wave, and isovolumic relaxation time (IVRT), and the TEI index [(isovolumetric contraction+relaxation time)/ejection time].All patients also received ACE inhibitor or AT1 blocker.

**Results**: after six months of follow up statistical significance was found in group receiving amiodarone (LVEDd, LA size, EF, E/A ratio, IVRT) comparing to the other groups. Baseline TEIindex was similar(0,72; 0,76; 0,74), but after six months it was significantly reduced in amiodarone group. 0,56 vs. 0,67 0,69;p<0,05), and it significantly changed comparing to the baseline.

Conclusion: TEI index remained pathological in all groups, but improved significantly in amiodarone group. Other measured parameters improved significantly in this group - we can conclude that amiodarone therapy after successfull cardioversion from chronic AF improves cardiac remodelling and diastolic function as well.