le tronc cérébral, dans la région du noyau du tractus solitaire qui régule les variations du tonus sympathique.

**Conclusion** — à l’âge de 3 mois, les rats SHR et SHHF présentent : (i) des résistances périphériques déjà très élevées, (ii) peu de retentissement cardiaque mais (iii) un remodelage cérébral marqué avec des variations de l’activité de centres régulant le tonus sympathique.

M002

**MOLECULAR IMAGING OF CARDIAC FIBROSIS WITH A NEW FLUORESCENT PROBES DIRECTED AGAINST MMPs**

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Fibrosis plays a central role in maladaptive remodelling processes, especially in the context of cardiovascular diseases. The fibrotic state depends on the balance between matrix metalloproteinases (MMPs) and their inhibitors, which alter the composition of extracellular matrix. Despite the necessity to localise and quantify fibrosis during cardiovascular diseases, only few biological markers of tissue fibrosis exist. Moreover none of them can evaluate fibrosis, in real time, in vivo. Therefore we developed an optical molecular probe (FR91) aimed at targeting cardiac matrix remodeling, with the innovative property of becoming fluorescent after cleavage by both MMP-2 and MMP-14. The present study was designed to validate this probe in cellular and animal models of MMP-2/MMP-14 activation and of fibrosis.

Regarding cellular models, murine fibroblasts (3T3) were exposed to 20 ng/ml TGF-b 1 for 24h. RT-PCR and zymography demonstrated increased MMP-2 and MMP-14 expression and activity. Immunofluorescence (IF) showed that 3T3 cells were positive for both MMPs, and this MMP IF signal colocalized with FR91 labelling.

Regarding animal models, C57BL/6J mice were subjected to Aortic Stenosis (AS; constriction of the thoracic aorta to 30-35% of its basal diameter). After 3 weeks, increased aortic pressure was confirmed and the heart taken out. We observed an increase by 60% of the left ventricular (LV) mass, and a doubling of cardiomyocyte size. Histological analysis showed a 8 fold higher collagen content in AS mice compared to controls. MMP-2 expression (PCR) was doubled while its activity (zymography) was strongly increased. In parallel MMP-14 expression and activity were also increased. These changes were associated with a concomitant increase in LV fluorescence for FR91 (assessed ex vivo), which was significantly higher in AS vs. control mice. This increased FR91 fluorescence observed in AS mice disappeared after incubation with EDTA which inhibits MMPs activity.

Thus, this study demonstrates that FR91 is a specific probe for the detection of increased MMP-2 and -14 activity and may be a unique tool to selectively detect cardiac fibrosis. Further experiments will test the capacity of FR91 to detect cardiac fibrosis in vivo.

M003

**REVERSE REMODELING AFTER TRIVENTRICULAR PACING IN REFRACTORY HEART FAILURE: A TDI AND 3D ECHOCARDIOGRAPHY STUDY**

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**Background** — In refractory heart failure, biventricular pacing improves prognosis and quality of life by reversing the left ventricular (LV) remodeling. We tested the hypothesis that triventricular pacing (TriV, 2 leads in the right ventricle and 1 lead in the coronary sinus) would better improve LV volume and function that does biventricular pacing (BiV).

**Methods and Results** — 15 consecutive heart failure patients (ischemic n=10 and non ischemic heart disease n=5) meeting the European criteria for cardiac resynchronization were imaged from 1 apical 3D acquisition in conventional and tissue Doppler modality (Vivid 7, GE Healthcare). LV volumes, EF and standard deviation in time to peak systolic velocity (modified Yu criteria from 6 segments) were measured before implantation and at 3-month F/U in triventricular and biventricular septal pacing. By ANOVA, biventricular septal pacing reduced LV volumes and improved EF compared to baseline (see figure). The additional significant EF enhancement found with triventricular configuration (p<0.05, see figure) was due to better tissue Doppler imaging synchronization (Standard deviation was 44±20ms, 36±12ms and 28±15ms at baseline, biventricular and triventricular septal pacing. By ANOVA, biventricular septal pacing reduced LV volumes and improved EF compared to baseline (see figure). The additional significant EF enhancement found with triventricular configuration (p<0.05, see figure) was due to better tissue Doppler imaging synchronization (Standard deviation was 44±20ms, 36±12ms and 28±15ms at baseline, biventricular and triventricular septal pacing.

**Conclusion** — In this pilot study, triventricular pacing demonstrates superior left ventricular reverse remodeling and intraventricular coordination than does biventricular pacing in patients with refractory heart failure.