Creation of bioartificial myocardium using elastomeric cardiopatch associated with nanobiotechnologies

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WG5. EU COST Action, Cooperation in Science & Technology
HEART FAILURE IN EUROPE
Total population 750 millions

• Around 14 million people in Europe have heart failure and its incidence is increasing (expected 30 million in 2020)

• More people are living to an old age, and more are surviving a heart attack but with damage to the heart
PREVALENCE of HEART FAILURE in USA

(total population: 320 millions)
VENTRICULAR REMODELING IN CHRONIC HEART FAILURE

Ventricular chamber dilatation and spherical deformation are important causes of morbidity and mortality of patients with congestive heart failure.
Spherical Shape in Heart Failure

Normal heart  Dilated LV
Tissue Engineering Cardiopatch

Goal of the Study

• Creation of biomimetic Cardiopatch to reduce fibrosis and the size of infarct scars in chronic ischemic disease

• Material: semidegradable membranes manufactured with elastomeric polymers and nanobiomaterials associated with stem cells
METHODS

• Cardiopatch was evaluated in a sheep ischemic model

• Biohybrid templates were created using elastomers (Polycaprolactone) and self-assembling peptide nanofibers (Puramatrix)

• Adipose progenitor stem cells (APC) were introduced inside the porous 3D membranes

• Cardiopatch was surgically grafted onto left ventricular postinfarct scars
Porous Cardiopatch seeded with hydrogel puramatrix and adipose tissue stem cells
Partially degradable: Caprolactone Methacryloxyethyl ester
Echocardiography: Strain Evaluation

Distortion of ventricular wall

Normal LV

Lateral + Apical infarction
Scaffolds with cylindrical orthogonal pores

Polycaprolactone scaffolds with spherical pores
Myocardial Infarct at 6 months

Without Treatment

With CARDIOPATCH
MAGNETIC RESONANCE IMAGING following Gadolinium IV injection

Myocardial infarct without treatment

Myocardial infarct treated with Cardiopatch
**MAGNETIC RESONANCE IMAGING**

**3D MYOCARDIAL INFARCT SIZE / LV MASS**

*(6 month follow-up)*

<table>
<thead>
<tr>
<th>GROUP</th>
<th>LV MYOCARDIAL MASS</th>
<th>INFARCT 3D SIZE</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROL</td>
<td>92 ± 5 cm³</td>
<td>13.7 ± 3 cm³</td>
<td>14.7 %</td>
</tr>
<tr>
<td>CARDIOPATCH</td>
<td>102 ± 7 cm³</td>
<td>6.4 ± 2 cm³</td>
<td>6.2 % *</td>
</tr>
</tbody>
</table>

* P < 0.05 vs control group
Histological Analysis

Figure X. Histological analysis of sheep hearts treated with adipose tissue derived progenitor cells (ATDPCs) loaded in a CLMA (A-C) or PEA bioimplant (D-E). ATDPCs were labeled with RFP (red). (A and E) Immunostaining against RFP shows presence of ATDPCs (red) in the myocardium scar and some of them integrated in the vessels as indicated by GSLI B4 isolectin staining (green). See insert details in B. (C and F) Immunostaining against RFP (red) and troponin I (green) shows presence of ATDPCs in the bioimplant (C) and in the myocardium (F) indicating migration of the implanted cells. (D) GSLI B4 isolectin staining (green) demonstrated presence of vessels in the bioimplant. Arrowheads indicate vessel connection between myocardium and bioimplant. Nuclei were counterstained with DAPI (blue). Scale bars = 100 μm.
RESULTS

- MRI and echocardiography showed at 6 months reduction of the infarct size in Cardiopatch group and improvements in systolic and diastolic functions.

- Histology showed stem cells inside the patch, into the infarct scars and the myocardium in cardiopatch group. Stem cells contributed to the formation of a capillary network between patch and myocardium.
Conclusions

• Postischemic ventricular dilatation and adverse remodeling raises the need to assist the heart to decrease ventricular wall deterioration

• This study shows that myocardial tissue engineering plays a key therapeutic role due to its capacity to replace extracellular matrix in postinfarct scars
Clinical Translation

Elastomeric membranes & nanotechnologies may contribute for the creation of Bioartificial Myocardium and Cardiowrap bioprostheses for ventricular support and myocardial repair.
INDICATIONS FOR BIOARTIFICIAL MYOCARDIUM

- ISCHEMIC HEART DISEASE
- DILATED CARDIOMYOPATHY
- PEDIATRIC CARDIOPATHIES
- DIABETIC CARDIOMYOPATHY
- RV DYSPLASIA
- CHAGAS’ HEART DISEASE
  (American Trypanosomiasis)
- PATCH for
  VENTRICULAR RESTORATION
HELICAL LOOP TO RESTORE CONICAL SHAPE IN DILATED HEARTS

European Patent 2 422 823, 2014
3D PRINTING for Cardiopatch & Cardiowrap
Local Myocardial Treatments

- Epicardial: surgical or endoscopic injections
- Epicardial: scaffold membranes
- Intravascular: catheter via coronary artery or vein
- Endocardial: intraventricular catheter
CATHETER FOR ENDOVENTRICULAR CELL DELIVERY
CATHETER - ELECTRODE
stabilizing by vacuum the infarct area
Catheter Cell-Fix
Simultaneous identification and injection - Electrophysiological infarct detection (R wave micro-voltage and decreased slew rate)

Immobilization (by suction) the treated area avoiding needle retraction and LV wall perforation

Improvement of cells retention
Acellular Tissue Engineering

• Acellular biomaterials can stimulate the local environment to repair tissues without the regulatory and scientific challenges of cell-based therapies

• Engineering hydrogels become extracellular matrix, an emerging therapeutic approach in cardiac repair