Creation of bioartificial myocardium using elastomeric cardiopatch associated with nanobiotechnologies

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WG5. EU COST Action, Cooperation in Science & Technology

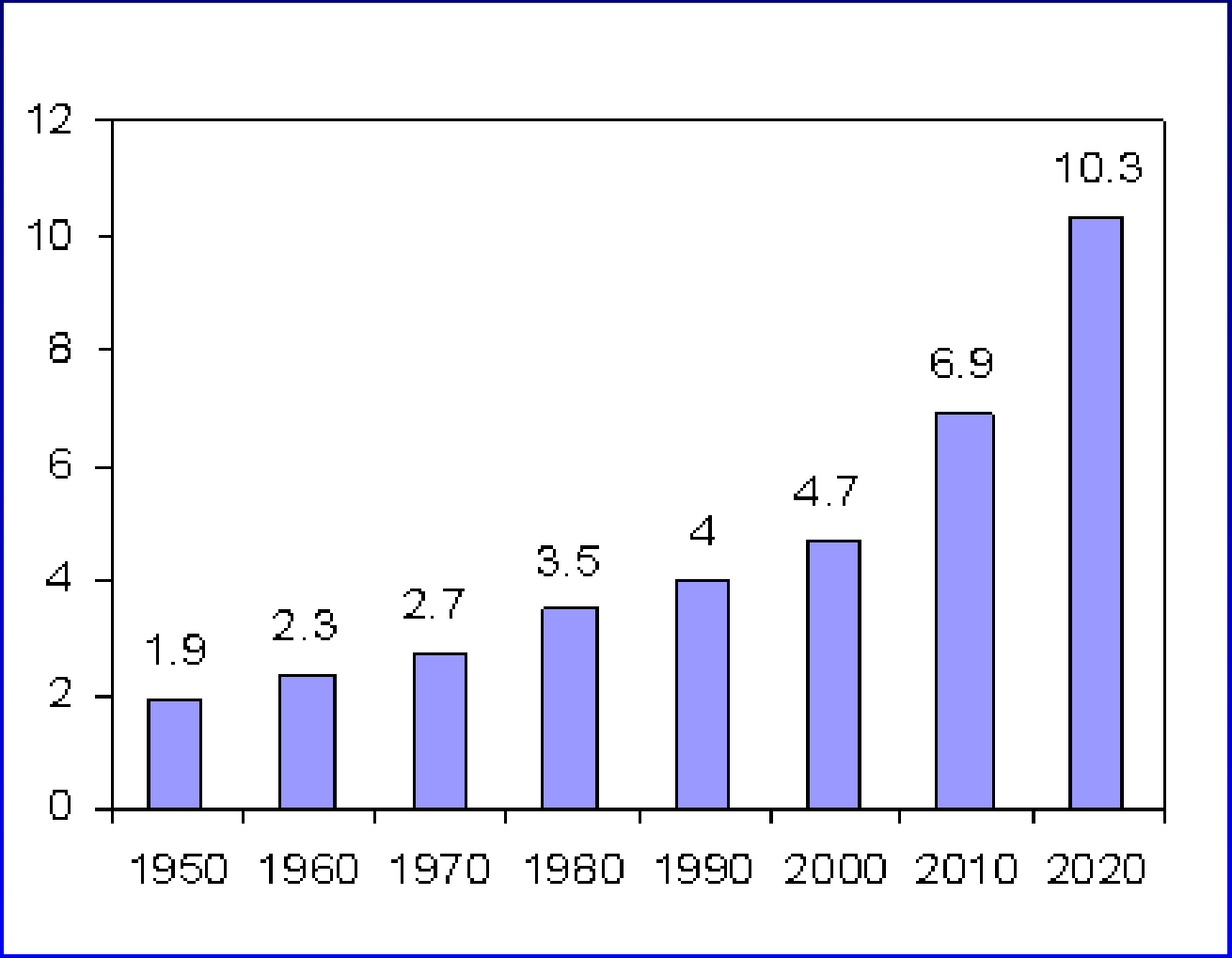
HEART FAILURE IN EUROPE

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)

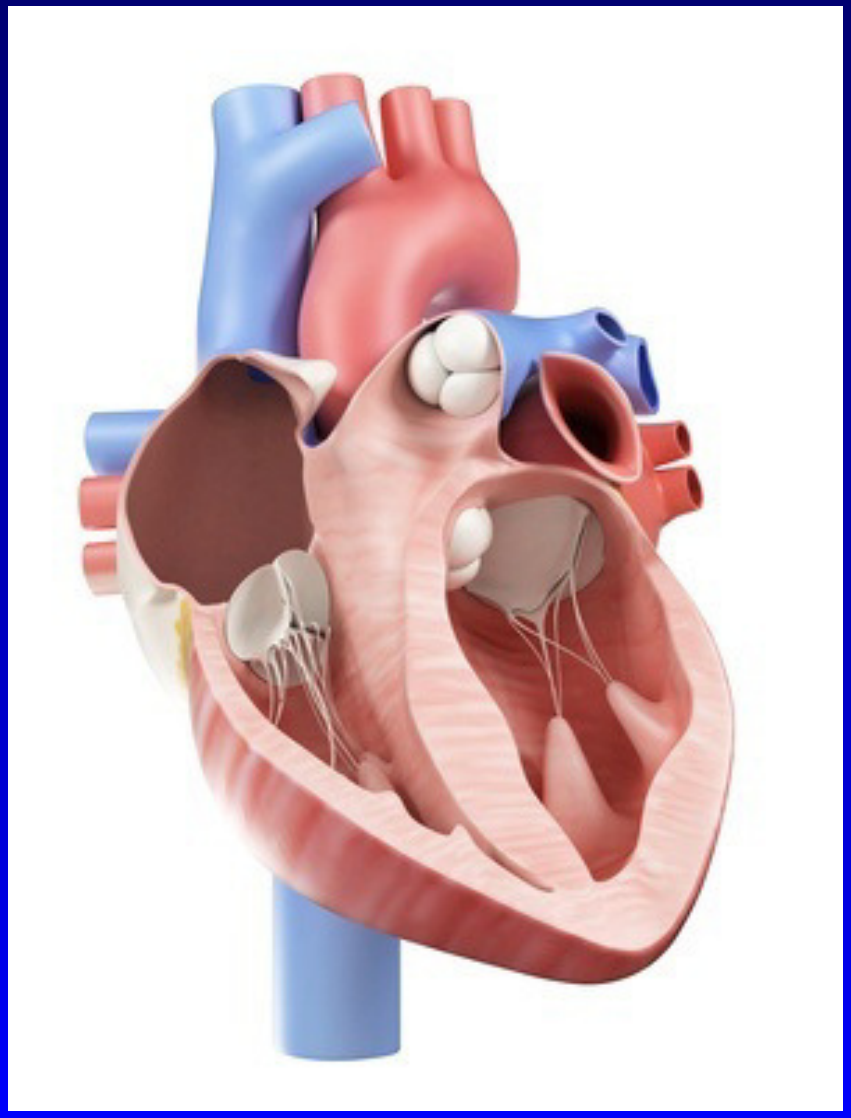


VENTRICULAR REMODELING IN CHRONIC HEART FAILURE

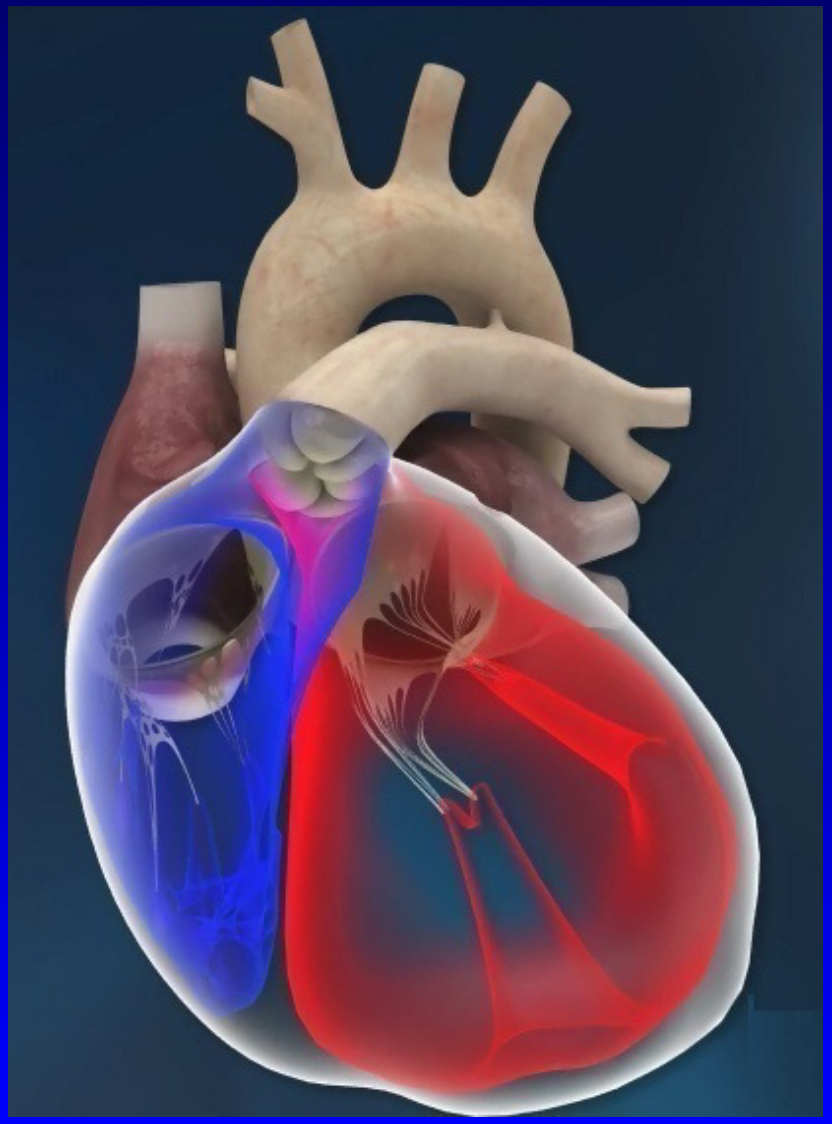
Ventricular chamber dilatation and spherical deformation are important causes of morbidity and mortality of patients with congestive heart failure

Spherical Shape in Heart Failure

Normal heart



Dilated LV



Tissue Engineering Cardiopatch

Goal of the Study

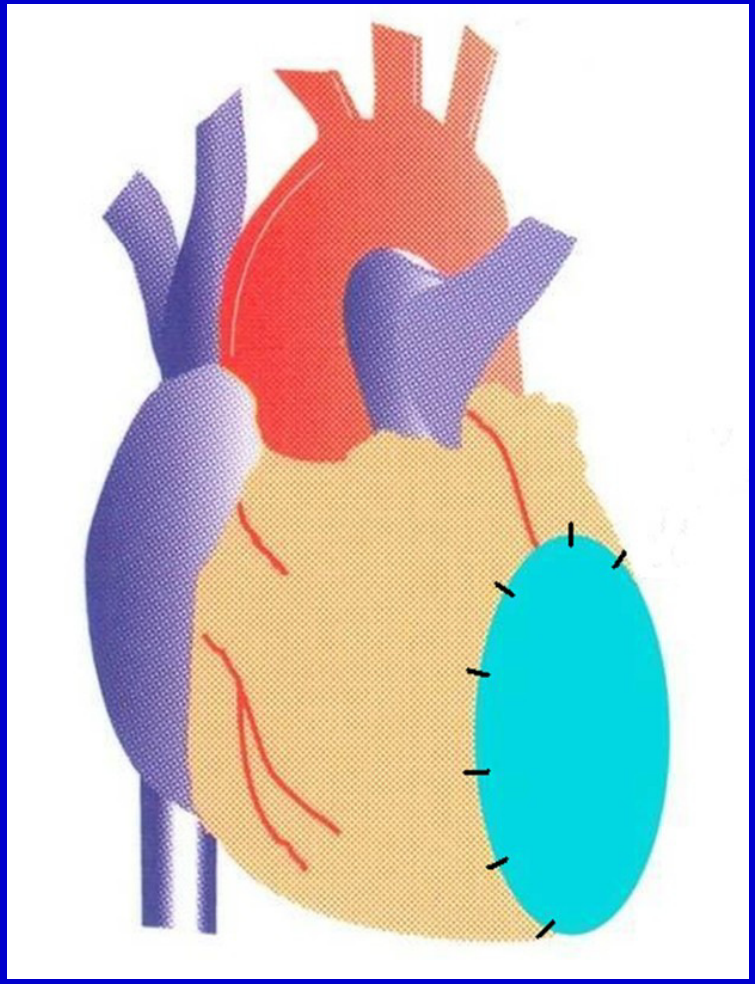
- Creation of biomimetic Cardiopatch to reduce fibrosis and the size of infarct scars in chronic ischemic disease

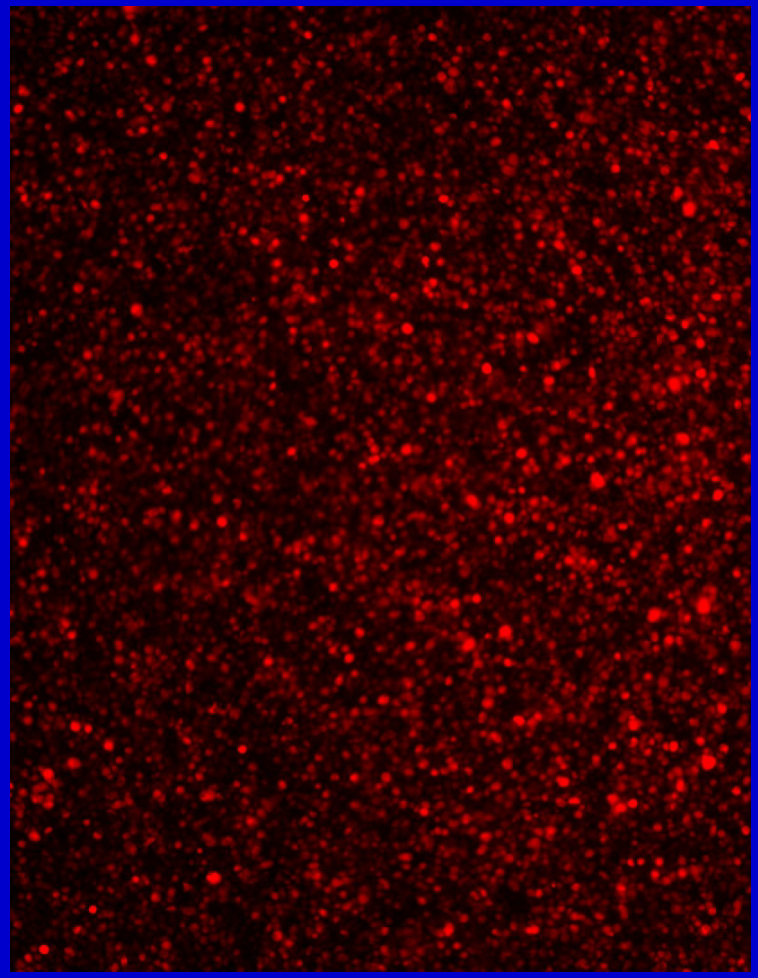
- Material: semidegradable membranes manufactured with elastomeric polymers and nanobiomaterials associated with stem cells

METHODS

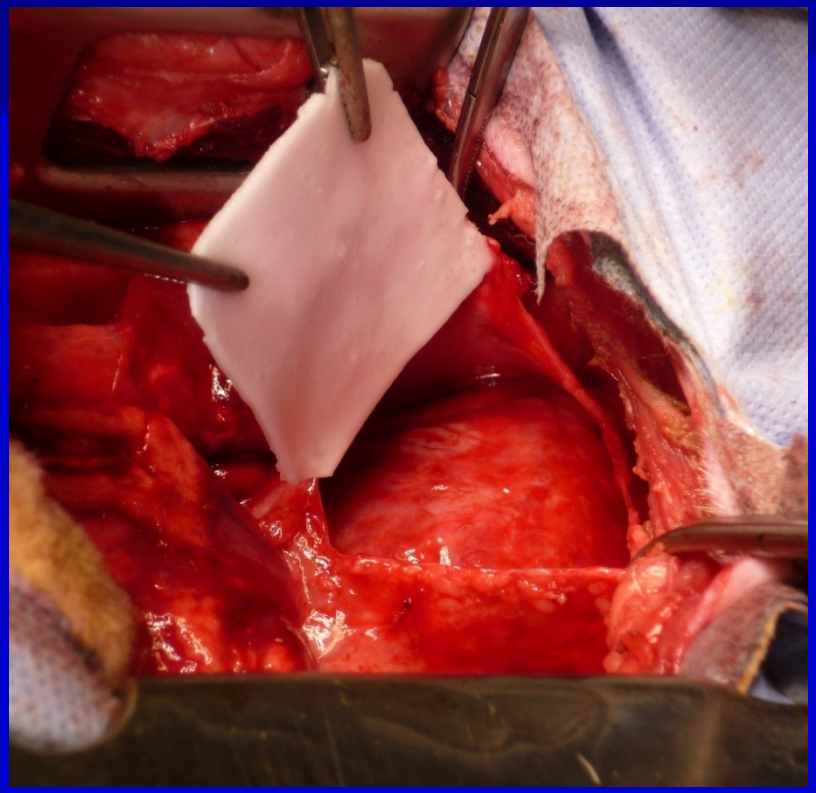
- Cardiopatch was evaluated in a sheep ischemic model
- Biohybrid templates were created using elastomers (Polycaprolactone) and self-assembling peptide nanofibers (Puramatrix)
- Adipose progenitor stem cells (APC) were introduced inside the porous 3D membranes
- Cardiopatch was surgically grafted onto left ventricular postinfarct scars

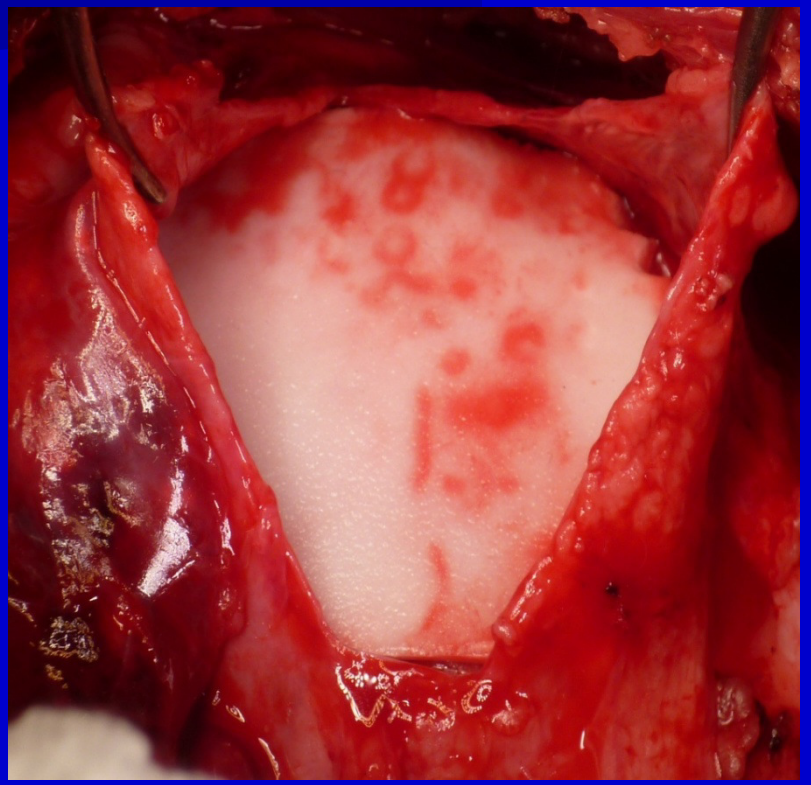
Porous Cardiopatch seeded with hydrogel puramatrix and adipose tissue stem cells





CARDIOPATCH SCAFFOLDS

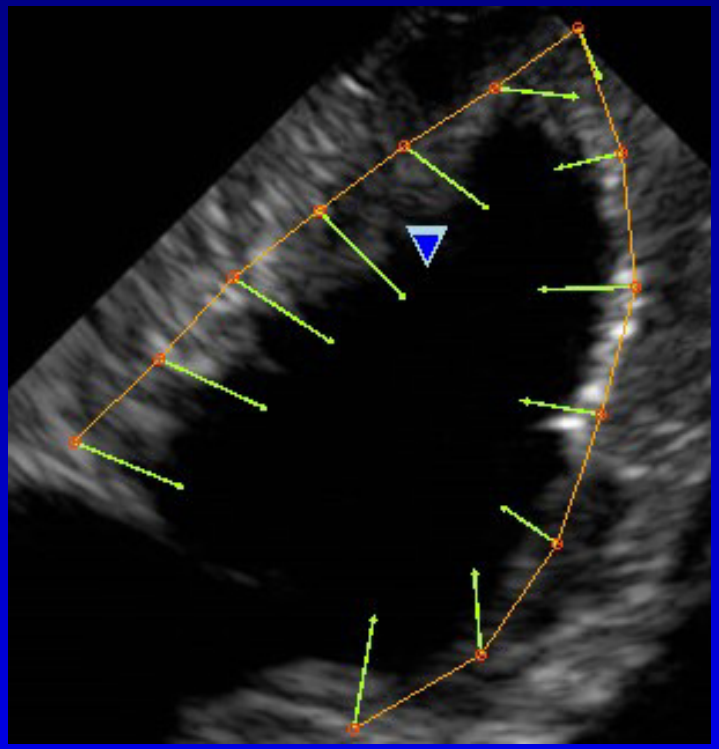




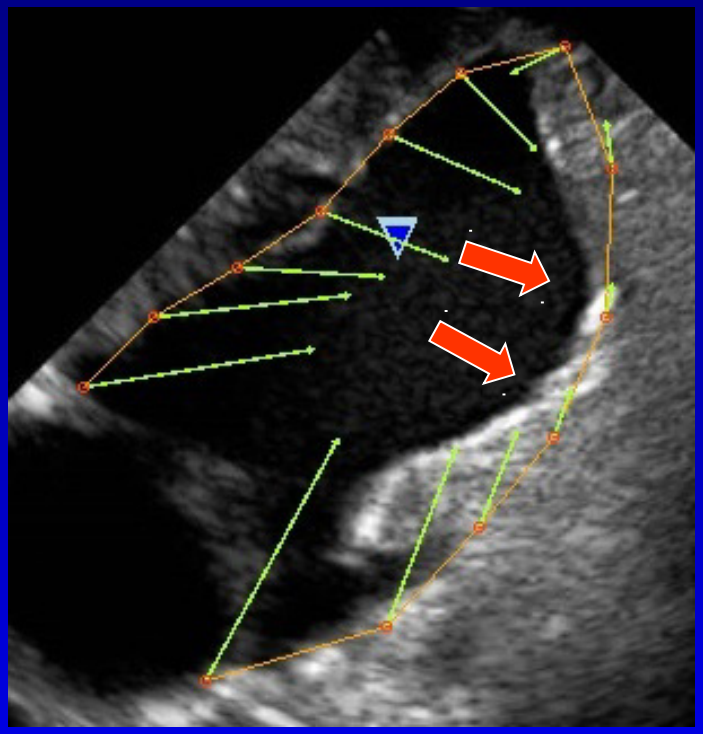
Partially degradable: Caprolactone Methacryloxyl ethyl ester

Echocardiography : Strain Evaluation

Distortion of ventricular wall

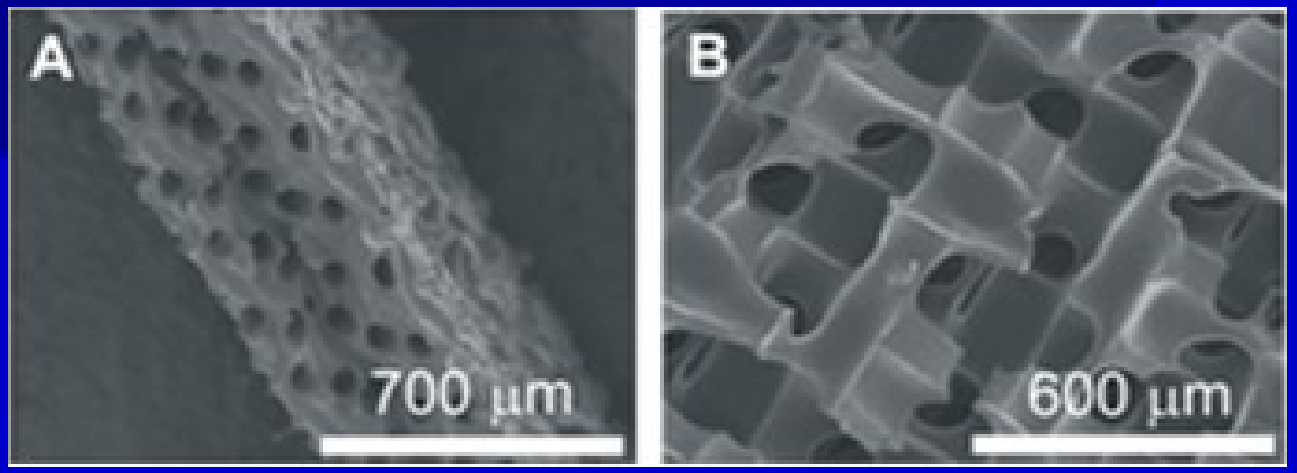


Normal LV

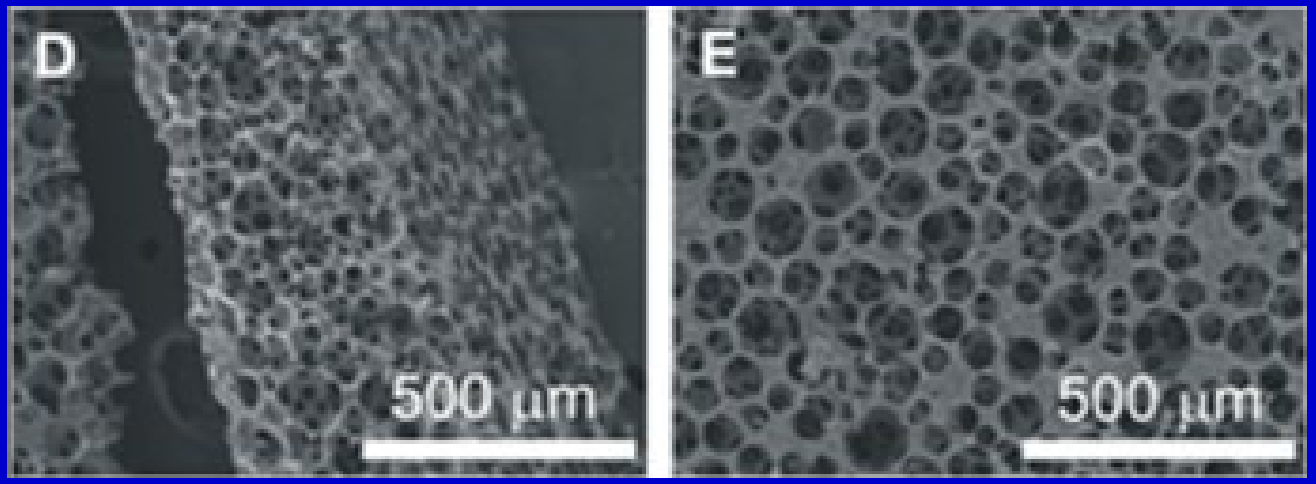


Lateral + Apical infarction

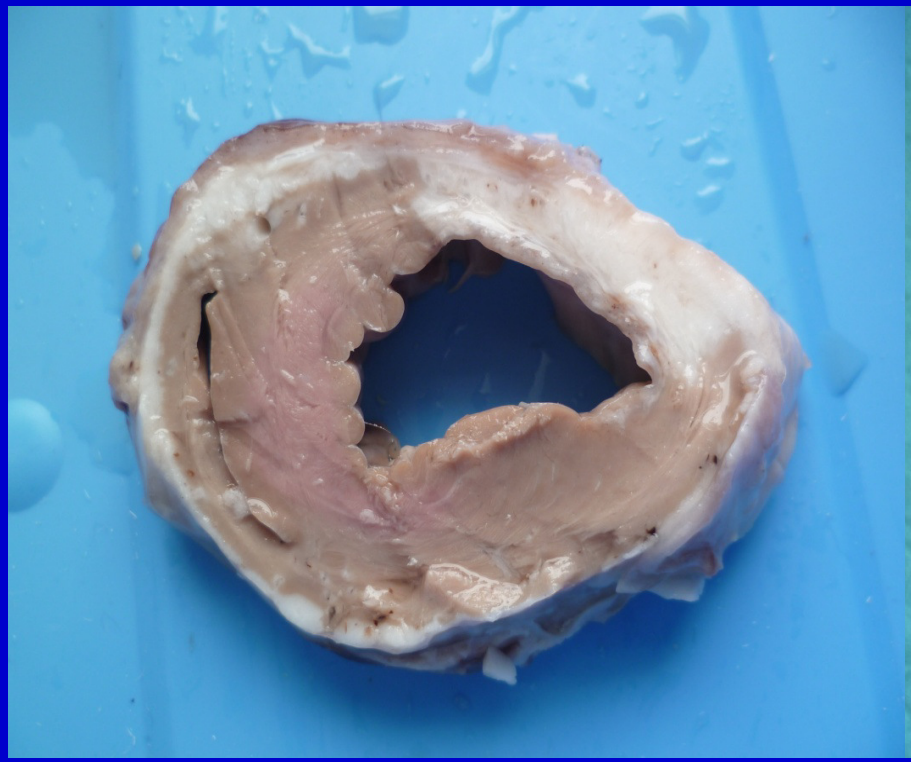
Scaffolds with cylindrical orthogonal pores



Polycaprolactone scaffolds with spherical pores



Myocardial Infarct at 6 months

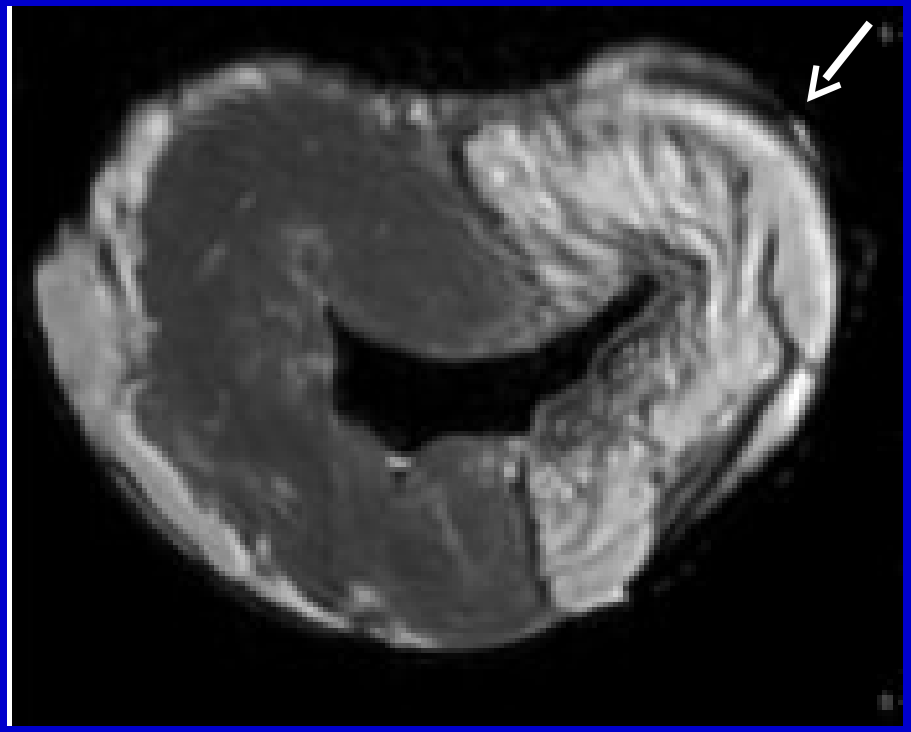


Without Treatment

With CARDIOPATCH

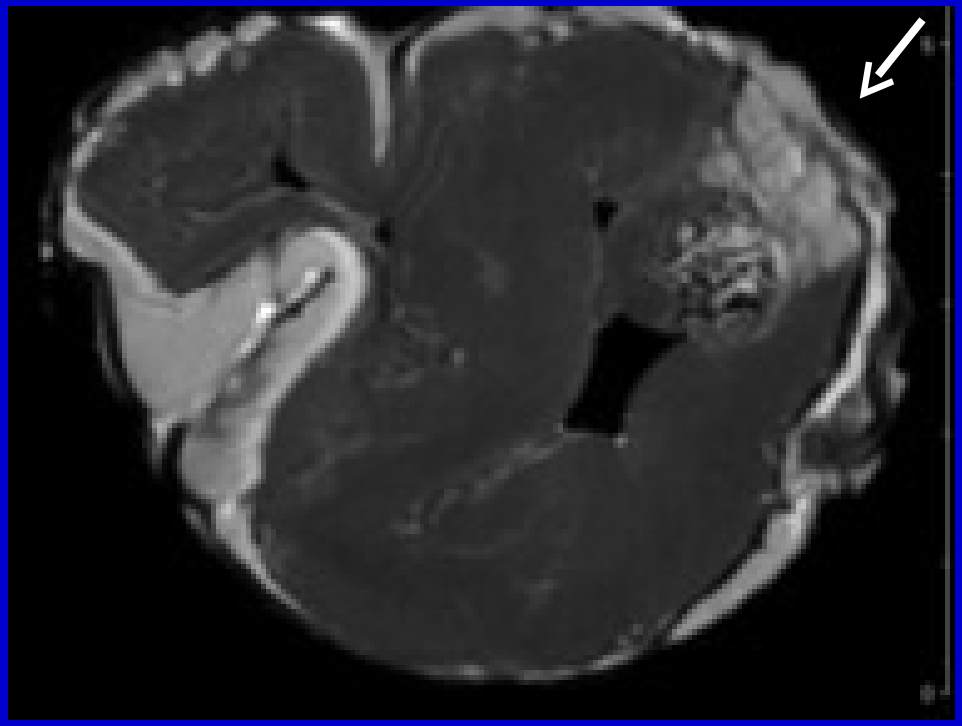
MAGNETIC RESONANCE IMAGING

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)

GROUP	LV MYOCARDIAL MASS	INFARCT 3D SIZE	%
CONTROL	92 ± 5 cm^3	13.7 ± 3 cm3	14.7 %
CARDIOPATCH	102 ± 7 cm^3	6.4 ± 2 cm3	6.2 % *

* P < 0.05 vs control group

Histological Analysis

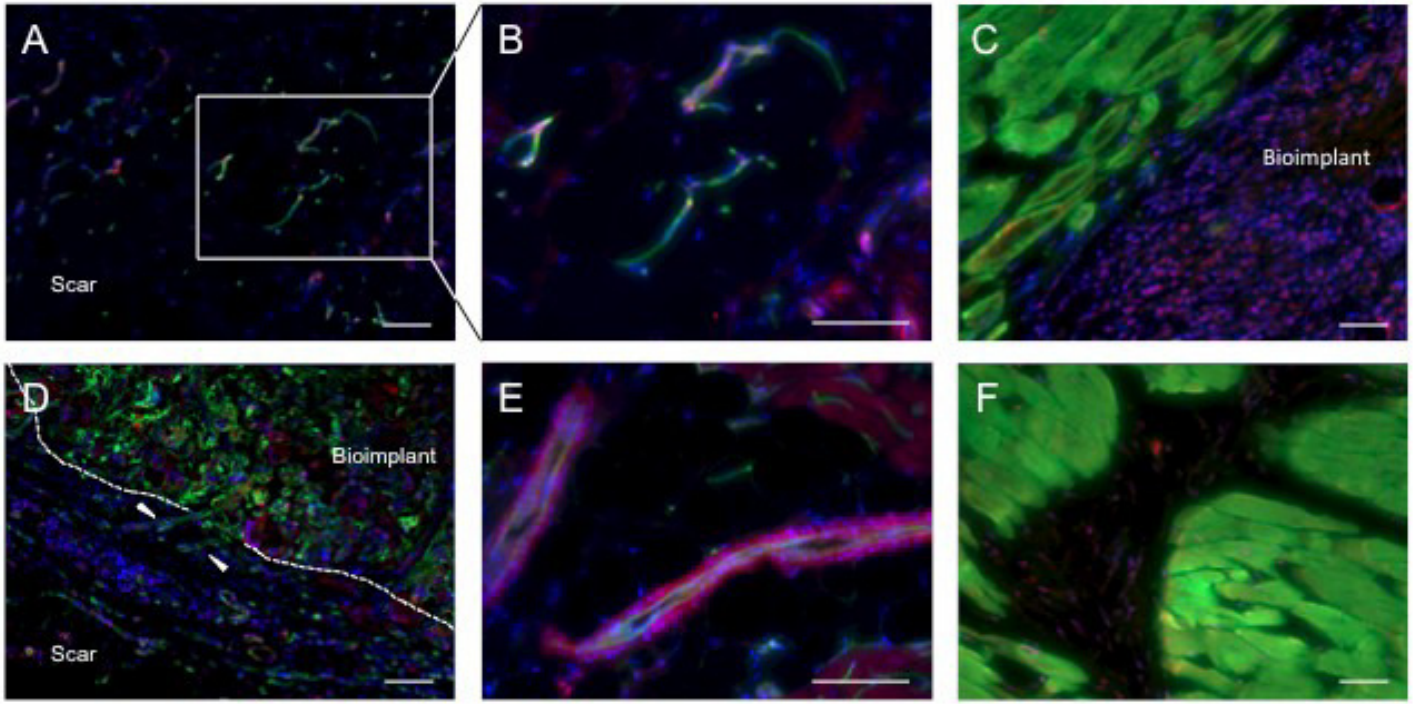


Figure X. Histological analysis of sheep hearts treated with adipose tissue derived progenitor cells (ATDPCs) loaded in a CLMA (A-C) or PEA bioimplant (D-E). ATDPCs were labeled with RFP (red). (A and E) Immunostaining against RFP shows presence of ATDPCs (red) in the myocardium scar and some of them 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

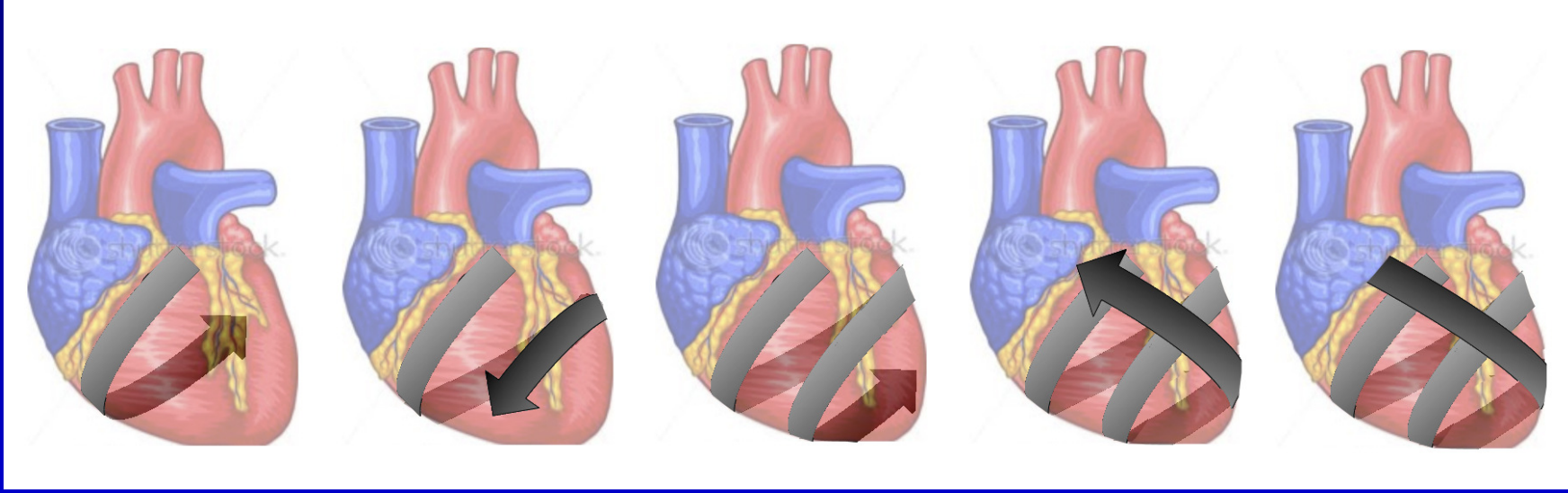
Clinical Translation

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



Chachques et al: Cardiowrap US Patent 8 968 417, 2015

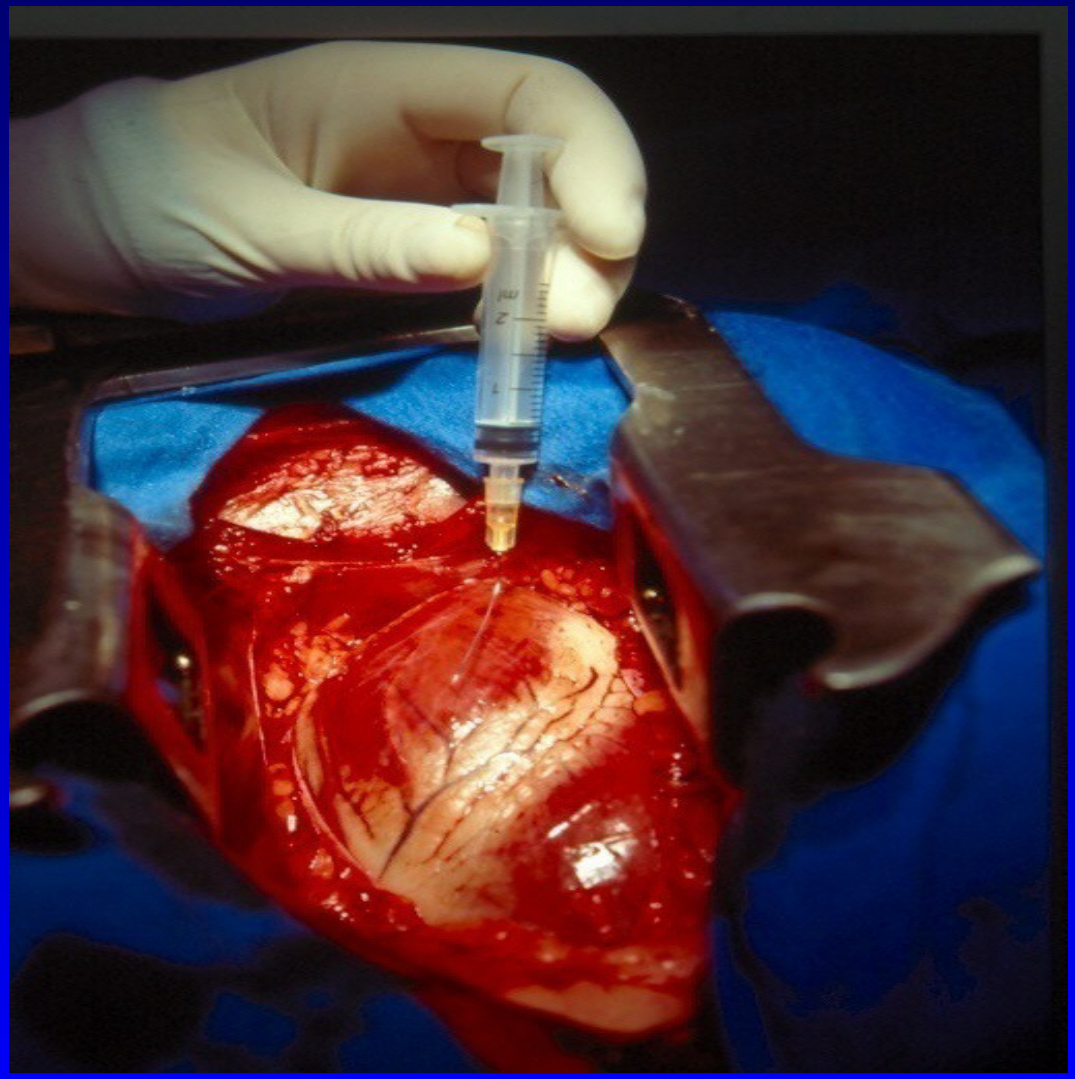
European Patent 2 422 823, 2014

3D PRINTING for Cardiopatch & Cardiowrap

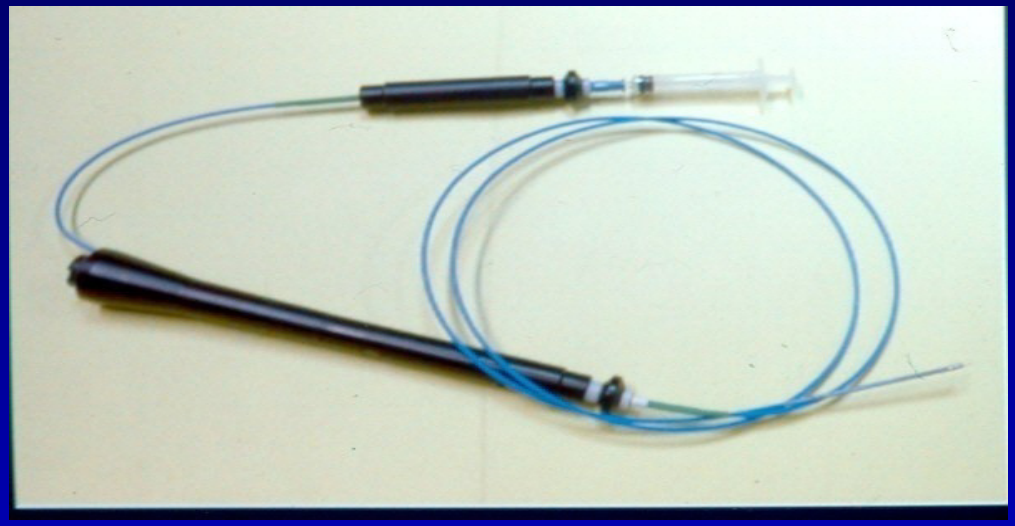
Local Myocardial Treatments

- Epicardial: surgical or endoscopic injections
- Epicardial: scaffold membranes
- Intravascular: catheter via coronary artery or vein
- Endocardial: intraventricular catheter

SURGICAL CELL IMPLANTATION

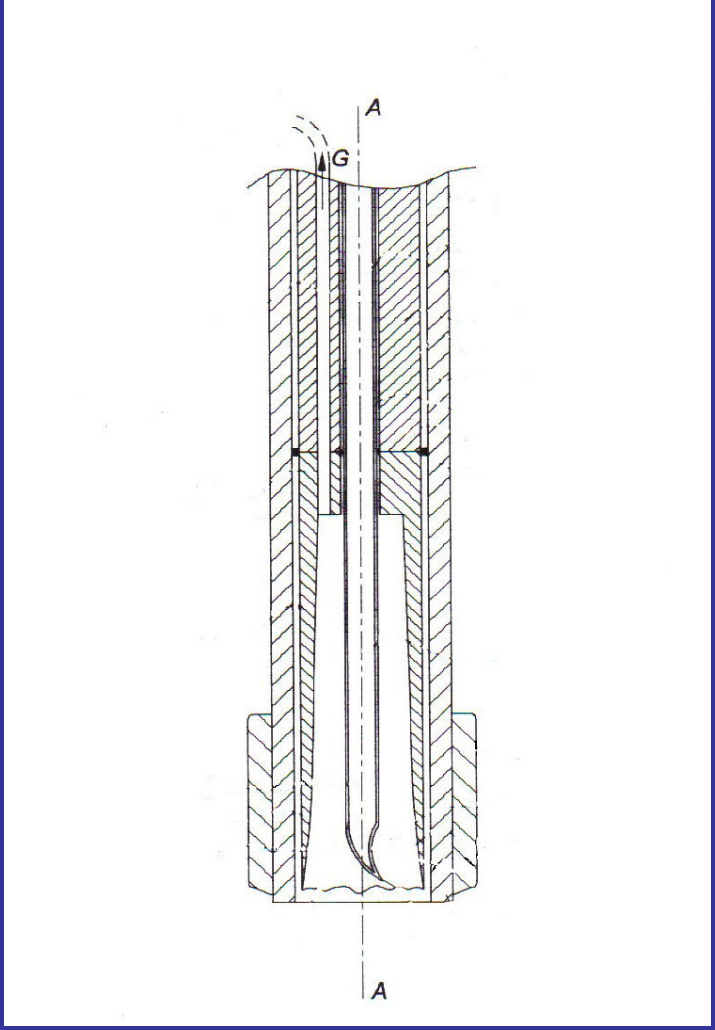


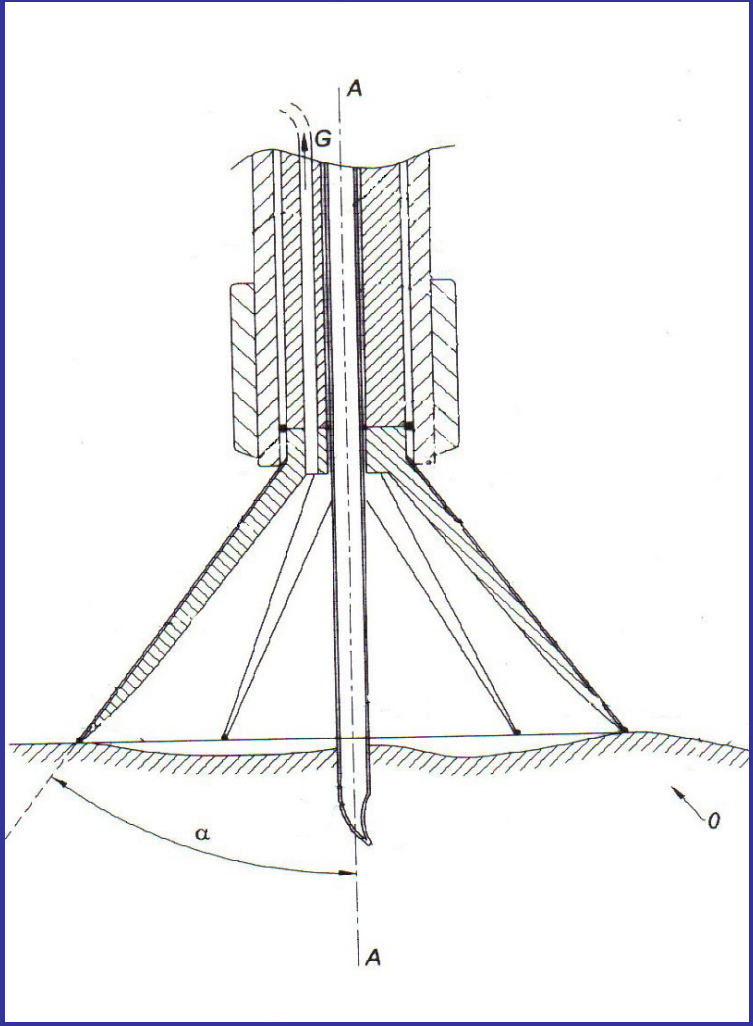
CATHETER FOR ENDOVENTRICULAR CELL DELIVERY



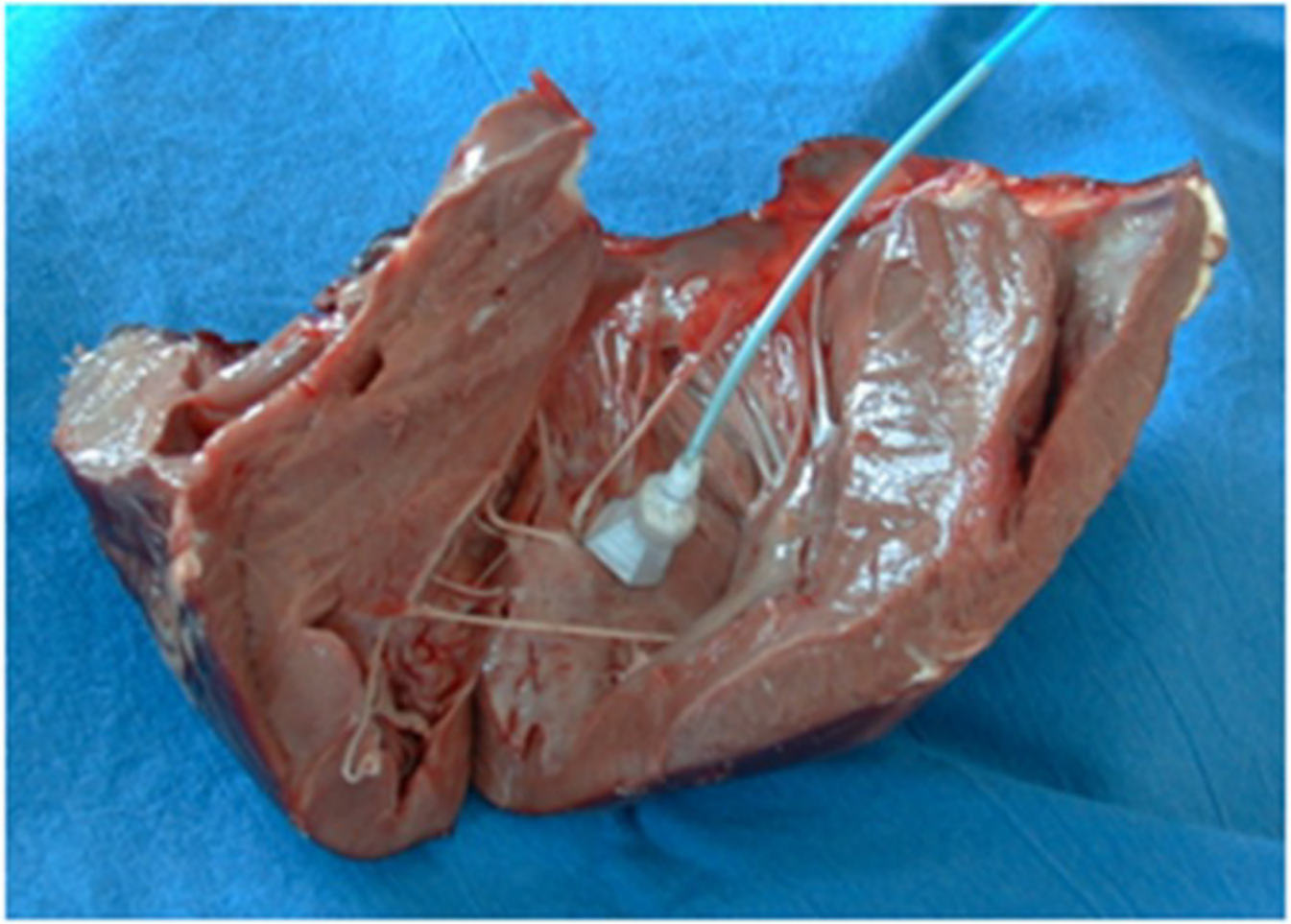
CATHETER - ELECTRODE

stabilizing by vacuum the infarct area





Catheter Cell-Fix



CATHETER CELL-FIX - ADVANTAGES

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