



A cardiopatch to regenerate the infarcted heart

What causes heart failure?

Heart failure is the main cause of death in the industrialized world. It induces up to 30% of death worldwide, i.e. over 15 millions deaths per year.

After myocardial infarction, cardiomyocytes are lost due to lack of vascularization.

Treatment options for infarction survivors are limited:

- advanced surgical or medical management is not always applicable to severe conditions,
- whole organ transplant suffers from a shortage of donors and limited life-span of implanted organs.

What is the hope of cell therapy for heart repair?

Cell-based therapy raises big hopes for the treatment of cardiac infarction and heart failure. Several cell types have shown promising therapeutic results in animal studies. Driven by these expectations, a number of clinical trials have been initiated, mainly using bone marrow stem cells or skeletal myoblasts.

However, the significant long-term improvement of cardiac function has not yet been achieved when using non cardiac committed cells.

Though cell-therapy seems to be safe, the modest beneficial effect is of short term, mainly due to paracrine effects, i.e. secretion of growth factors from cells before their disappearance.

Repopulating the damaged areas after myocardial infarction with new functional cardiac cells would be essential for the restoration of a functional contracting myocardium.

Why cell format delivery for efficient heart regeneration?

Transplanting cells using a syringe has proven ineffective. Indeed, more than 90% of the cells are lost when injected in a heart that contract 60 time per minute.

As a solution, tissue engineering strategies are under intense development. The goal is to seed cells into biomatrices composed of natural or synthetic proteins mimicking the extracellular environment to which cells can adhere and function in three dimensions.

Compared with other methods such as intra-myocardial injection, the advantages of delivering cells either seeded into biomatrices or admixed with liquid biomatrices that form a gel upon injection, are the following:

- increased cell retention
- improved colonization and integration of the tissue to be treated
- *in situ* differentiation into functional cardiomyocytes
- cardiac function outcomes
- incorporation of different cells types and growth factors that improve cell survival and function.
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Preclinical proof of concept

We have developed and patented a method to form cardiopatches composed of a fibrin gel for the efficient delivery of cardiac-committed cells to the infarcted heart tissue.

Fibrin patches are biodegradable, non immunogenic and have healing properties and are already used in clinical trials.

We have validated the use of cardiopatches into a rat model of myocardial infraction. We have shown that a cardiopatch applied onto the infarcted area of the left ventricle wall enabled cells to migrate into the tissue and improve heart function parameters (end systolic volume, end diastolic volume, ejection fraction).

Results published in: *Vallée JP et al. Stem Cells and Translational Medicine 2012, 2011(3).*

