



HAL
open science

Moderate deformation of cartilage micropellets in a fluidic custom-made device enhances the expression of chondrocyte markers

Noémie Petitjean, Marie Maumus, Gilles Dusfour, Patrick Cañadas, Christian Jorgensen, Pascale Royer, S. Lefloch, Danièle Noël

► To cite this version:

Noémie Petitjean, Marie Maumus, Gilles Dusfour, Patrick Cañadas, Christian Jorgensen, et al.. Moderate deformation of cartilage micropellets in a fluidic custom-made device enhances the expression of chondrocyte markers. International Society for Cell and Gene Therapy - ISCT 2021, May 2021, En ligne, United States. . hal-03440887

HAL Id: hal-03440887

<https://hal.science/hal-03440887>

Submitted on 22 Nov 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Introduction

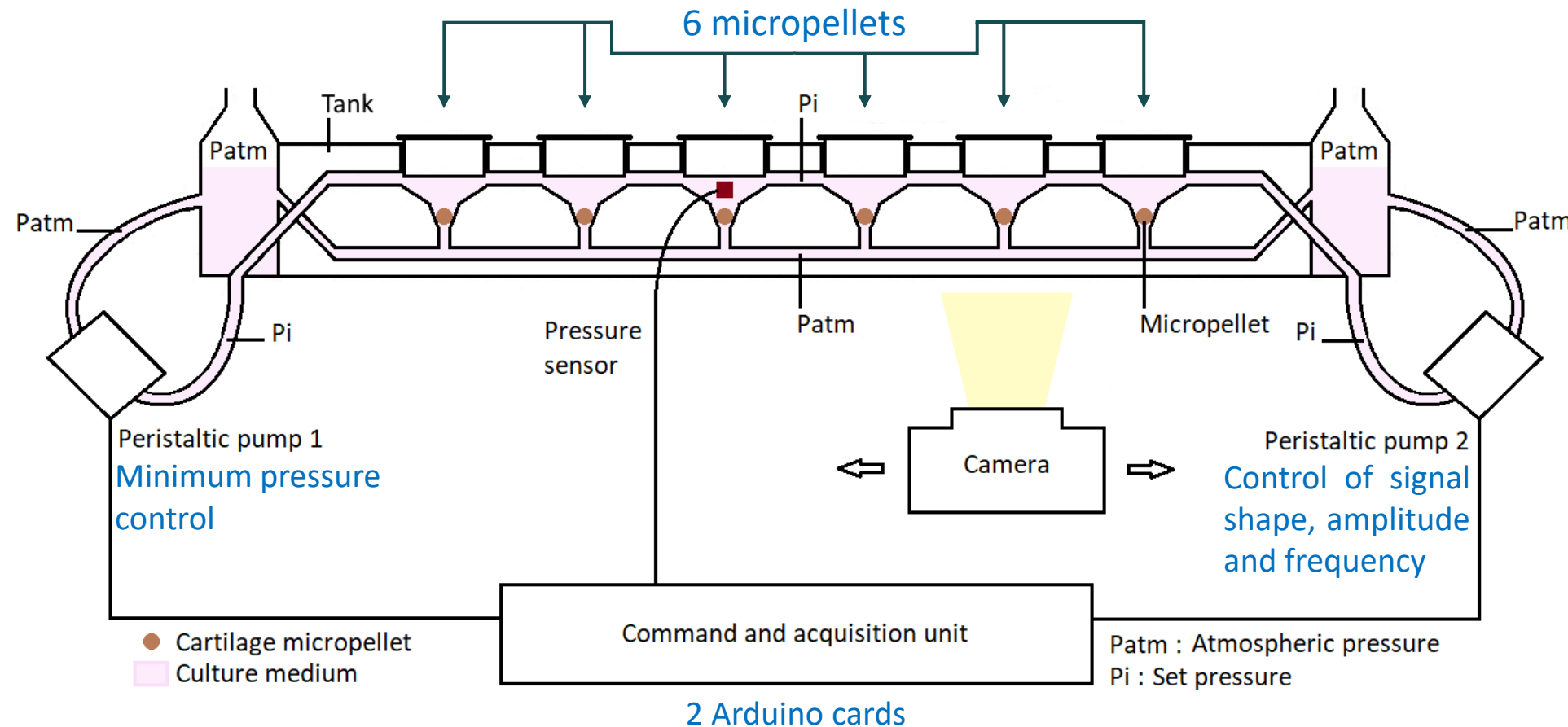
Cartilage engineering approaches are being developed for evaluating the repair of articular cartilage lesions but few of them have reached the clinics. One limitation of current approaches is the lack of mechanical stimulus. Cartilage micropellet is a well-known model of cartilage growth but no study has evaluated the impact of mechanical stimulation on their development by analyzing both their biochemical and biomechanical properties.

Objectives

We relied on the use of a **fluidic custom-made device** for **biomechanical stimulation and characterization** of mesenchymal stromal cells (MSCs)-derived **cartilage micropellets**.

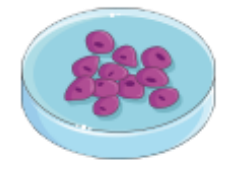
Methods

- The fluidic custom-made device:

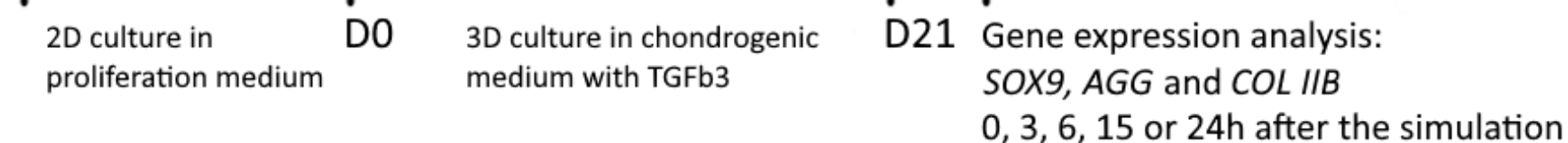


- Biomechanical stimulation:

Biomechanical stimulation with a square signal:
 15, 30 or 60 min
 0.25, 0.5, 1 or 2 Hz
 1.75, 3.5, 7 or 14 kPa



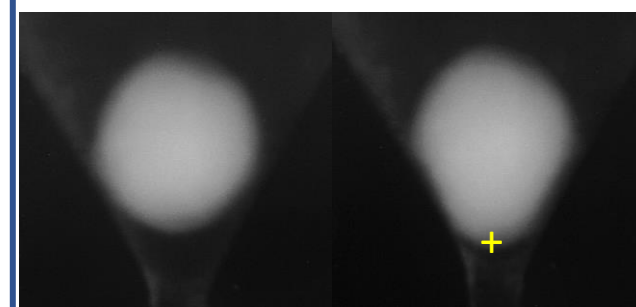
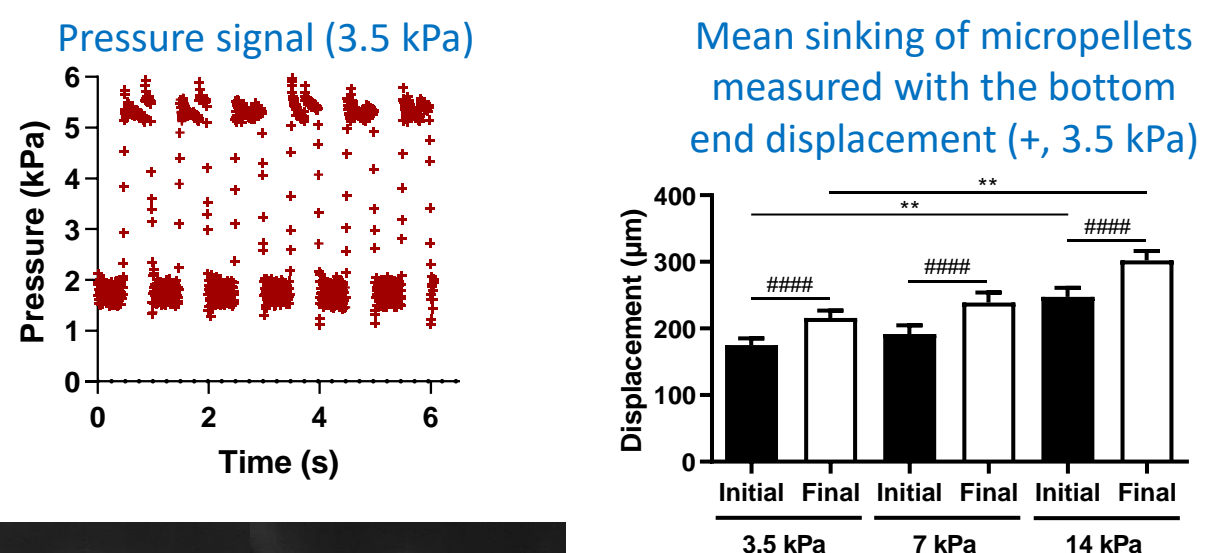
hBM-MSC expansion Pellet formation



Results

1/ Moderate and non destructive deformation of cartilage micropellets under biomechanical stimulation

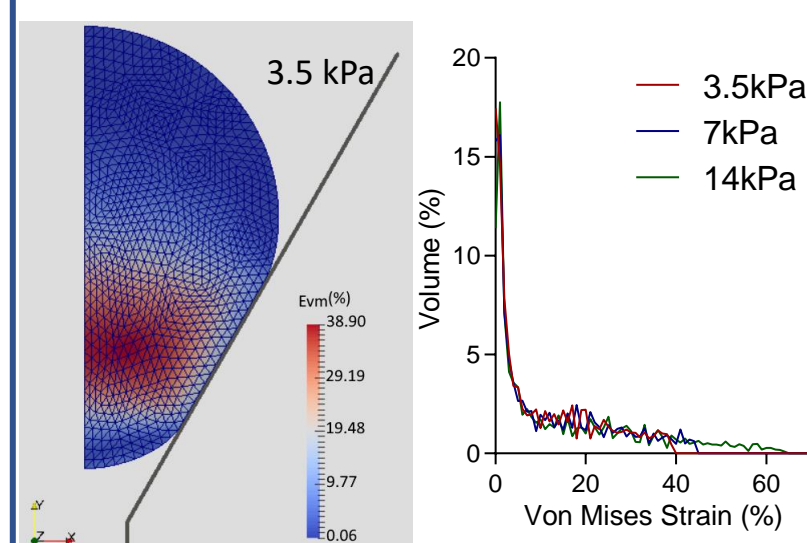
- Sinking of micropellets in their conical wells during biomechanical stimulation:



Micropellet sinking increases with the amplitude of pressure and stimulation time

- Deformation of micropellets in their conical wells during biomechanical stimulation:

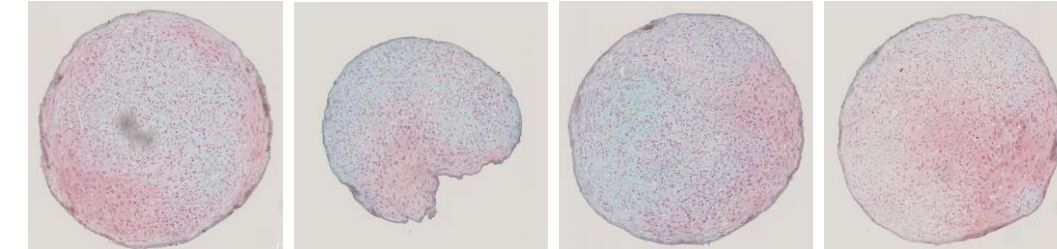
Distribution of Von Mises strain evaluated with a finite element model employing a neo-Hookean law



Von Mises strain can reach 38.90% at 3.5 kPa amplitude of pressure but 80% of the micropellet have strains < 20%

- Micropellet microstructure:

Safranin O staining of proteoglycans after biomechanical stimulation

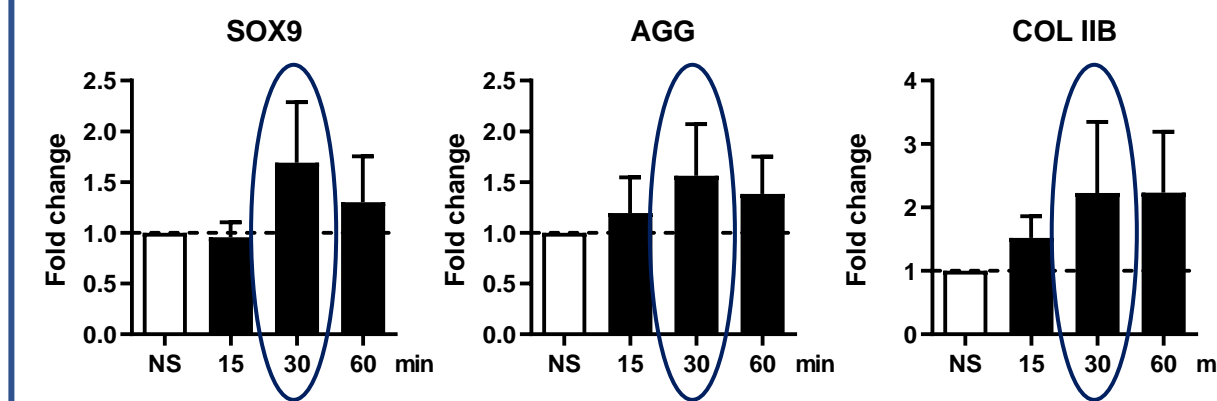


The microstructure of micropellets is not altered

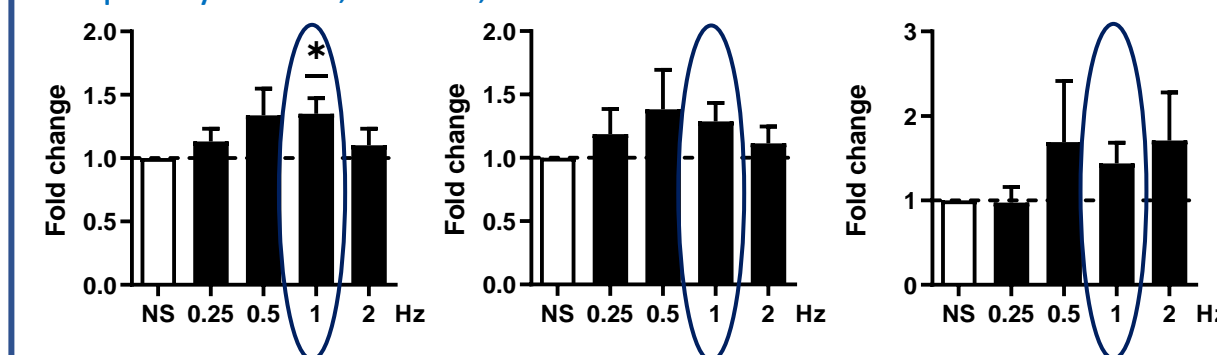
2/ Regulation of chondrocyte gene expression by biomechanical stimulation

- Chondrocyte gene expression 24h after biomechanical stimulation:

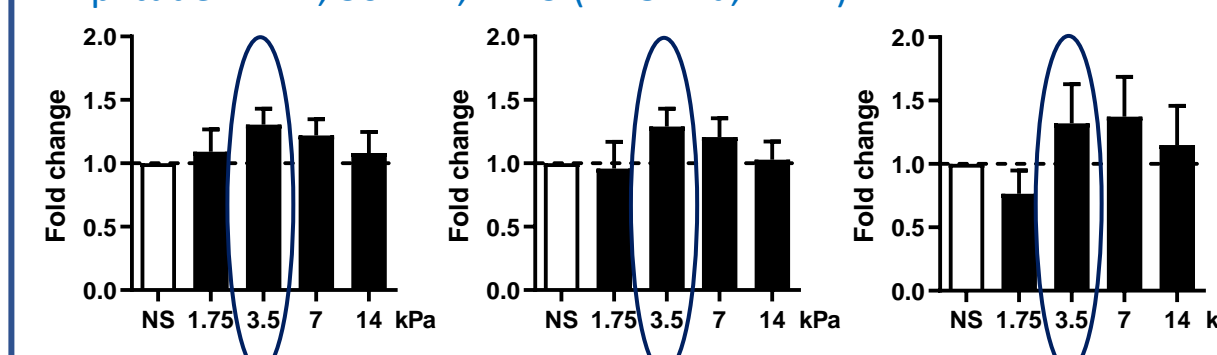
Duration : 7 kPa, 1 Hz, n = 5



Frequency : 7 kPa, 30 min, n = 7

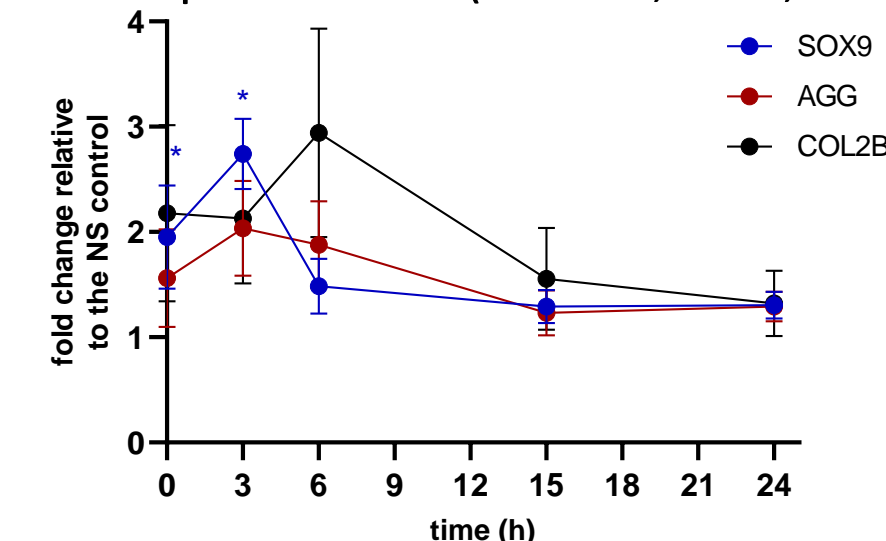


Amplitude : 1 Hz, 30 min, n = 9 (1.75 kPa, n = 4)



Higher expression of SOX9, AGG and COL IIB was measured at 3.5 kPa, 1 Hz, 30 min

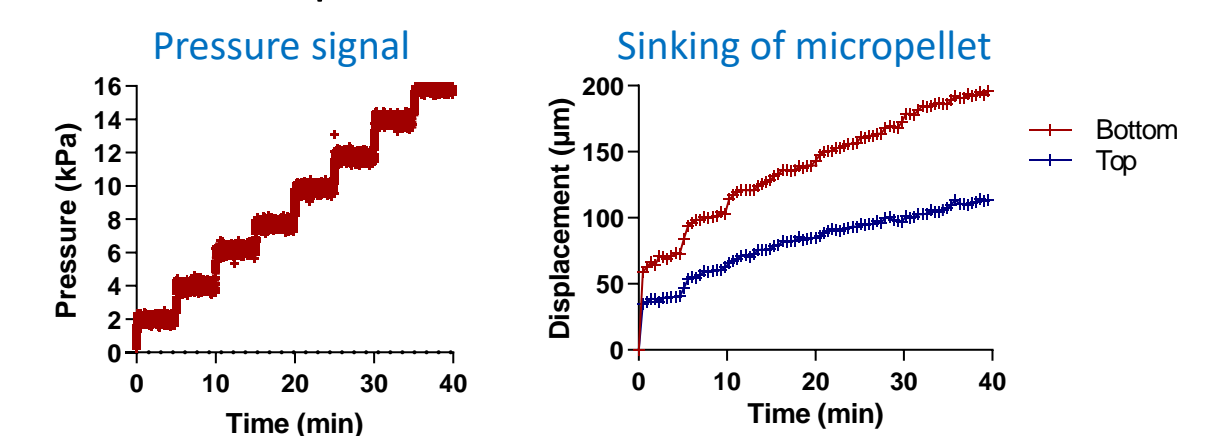
- Time-dependent analysis of gene expression for constant parameters (3.5 kPa, 1 Hz, 30 min):



Gene expression is upregulated at early time points (3h seems the best)

3/ Mechanical characterization of micropellets with the fluidic device

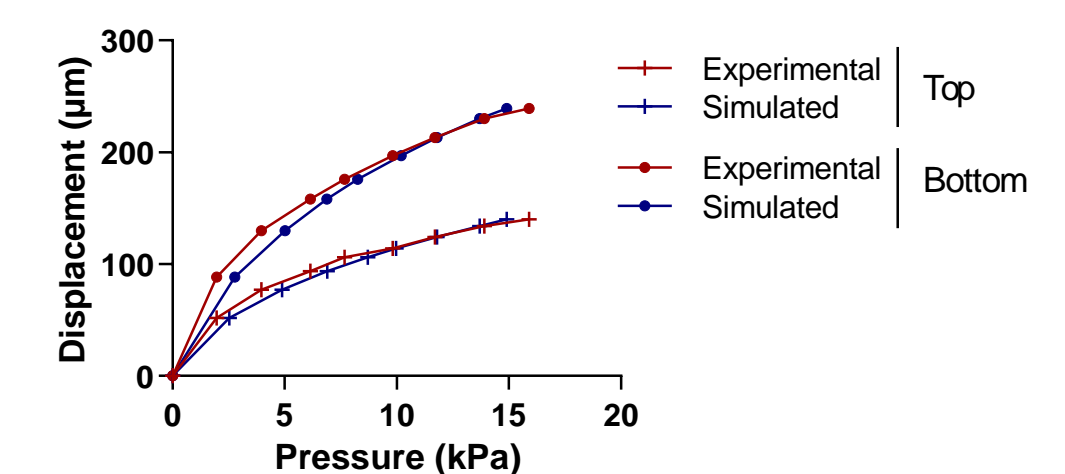
- Multi-creep test at D21:



- Determination of the mechanical properties at equilibrium by inverse analysis:

Experimental curves: Last point of each pressure step and normalization of the displacement with the radius of micropellets

Simulated curves: Estimated pressure from experimental displacements



A Young's modulus of 47.6 ± 26.2 kPa and a Poisson ratio of 0.46 ± 0.02 were obtained at the equilibrium

Conclusions

- The micropellets can be biomechanically stimulated in the fluidic device without being microstructurally altered
- The biomechanical stimulation enhances the expression of chondrocyte genes
- The mechanical properties of cartilage micropellets can be assessed in the device