PURPOSE. In osteoarthritis (OA), subchondral bone remodeling is increased leading to bone sclerosis. In a previous work, we have reported that osteoblasts coming from the sclerotic subchondral bone express a particular phenotype characterized by an increased production of insulin-like growth factor (IGF)-1, interleukin (IL)-6, IL-8, prostaglandin (PG)E₂, receptor activator of nuclear factor kappa-B ligand (RANKL), matrix metalloproteinase (MMP)-3 and a decrease of osteoprotegrin (OPG). We have investigated if these genes are mechanosensitive and the presence of the main mechanoreceptors in these cells.

METHODS. Osteoblasts were isolated from sclerotic (SC) or non-sclerotic (NSC) zones of OA subchondral bone of five men. After 28 days, osteoblasts in culture were surrounded by a newly synthesized matrix and formed a strong membrane. This osteoblasts-containing membrane was then placed onto a Flexercell Biopress plate and submitted to compression (10%) for 4 hours at the frequency of 1 Hz (Fig 1). Gene expression was evaluated by RT-PCR. Protein productions were quantified in culture supernatant by immunoassays (ELISA) or visualized by immunohistochemistry.

RESULTS. Compressions increased the expression of genes coding for IGF-1, IL-6, COX-2, RANKL, vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF-2), IL-8, MMP-3, MMP-9 and MMP-13 but decreased the expression of OPG in osteoblasts (p<0.01) in both SC and NSC. Type I collagen (COL1A1) and MMP-2 were not significantly affected by mechanical stimuli (Fig. 2). NSC osteoblasts were significantly more sensitive to compression than SC ones, and after compression, mRNA levels differences between NSC and SC osteoblasts were largely reduced or even abolished. In basal condition, SC osteoblasts expressed similar levels of integrin α5, αv, β1, β3 and CD44 than NSC ones, but 30% less connexin (Cx)43, an important mechanoreceptor. Immunohistochemistry analysis showed less Cx43 proteins in SC than NSC membranes (Fig. 3).

CONCLUSION. Cx43 plays a major role in osteoblast mechanotransduction. It is less expressed by SC than NSC osteoblasts. Further, Cx43 is decreased by compression in SC osteoblasts. This downregulation of Cx43 could be responsible for the decrease in mechanosensitivity of SC osteoblasts. This compression model offers new perspectives of research to explain the role played by mechanical stimuli in OA pathogenesis. This technology could also be used to investigate cartilage physiology and physiopathology under mechanical stress occurring in obesity or in ageing.