# MR molecular imaging of homing of Integrin-linked kinase-overexpressing mesenchymal stem cells after transplantation via coronary in Swine acute myocardial infarction model

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**Target audience:** radiologist and cardiologist

**Purpose:** Clinical studies have suggested that the effects of intravascular administration of mesenchymal stem cells (MSCs) on cardiac function in acute myocardial infarction (AMI) are less than expected because of the poor cell homing[1]. Some study have demonstrated that endogenous ILK may control the recruitment of endothelial progenitor cells (EPCs) to ischemic tissue[2]. It is urgent to identify and dynamically monitor transplanted cells in vivo for verification of effect of ILK gene on MSCs homing. The present study aims to in vivo detect the homing and migration ability of MSCs overexpressing ILK (ILK-MSCs) after transplantation via coronary in swine model of AMI using MR molecular imaging technique.

**Methods**: MSCs or ILK-MSCs（$5\times10^7$ cells）genetically modified with adenovirus containing GFP/ILK or GFP and labeled with ultrasmall superparamagnetic iron oxide(USPIO) were randomly transplanted into the ischemic myocardium via coronary artery 1 week after establishing the swine myocardial infarction model(6 swine per group) by ballon occlusion. The cell cardiac homing and migration were tracked in vivo at 24h, 3d, 1w and 2w after transplantation using MR molecular imaging on clinical 1.5T Philips MR scanner. The GFP expression was calculated from frozen section and the USPIO in transplanted cells was detected by prussian blue staining 2 weeks later. The data was statistically analyzed with Independent Sample t test for two group comparison using SPSS17.0 software.

**Results:** In vivo MR molecular imaging manifested in both groups that the hypointensity area （MSCs:89.68±4.61mm$^2$ vs. 80.06±5.47mm$^2$, $p<0.05$; ILK-MSCs: 102.3±4.22mm$^2$ vs.89.98±6.15mm$^2$, $p<0.05$）and signal intensity variation (MSCs: 666.0±48.23 vs.457.2±43.80, $p<0.05$; ILK-MSCs: 830.8±33.10 vs. 662.4±40.98, $p<0.05$) at 3d were larger/higher than those at 24h. The area (MSCs:97.60±4.05mm$^2$;ILK-MSCs:109.8±6.96mm$^2$) was increased($p<0.05$),but the intensity variation (MSCs:359.8±44.94;ILK-MSCs:473.6±44.85) was decreased 1 week later ($p<0.05$); the area (MSCs:32.52±7.65mm$^2$; ILK-MSCs:19.00±3.10mm$^2$) and intensity variation （MSCs:218.6±71.86;ILK-MSCs:108.6±77.87）were all decreased 2 weeks later compared to those at 1week ( $p<0.05$). The area and intensity variation of ILK-MSCs group was larger/higher in former 3 time points compared with those of MSCs group ($p<0.05$), but smaller/lower in 2 weeks ($p<0.05$) (Fig1). More GFP positive (84.0±8.8/field vs. 21.3±8.3/field<0.001) and prussian blue staining positive cells (275±54/field vs. 144±54/field, $p<0.001$) were found in ILK-MSCs group 2 weeks after cell transplantation (Fig2).

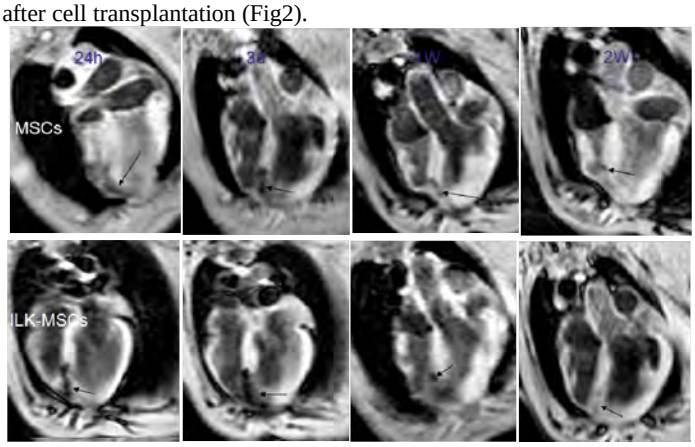


Figure1. On dynamic TW*I images, hypointensity area is detected in the anterior ventricular septum. The hypointensity area and signal intensity variation of ILK-MSCs group is larger/higher in former 3 time points compared with those of MSCs group, but smaller/lower in 2 weeks.

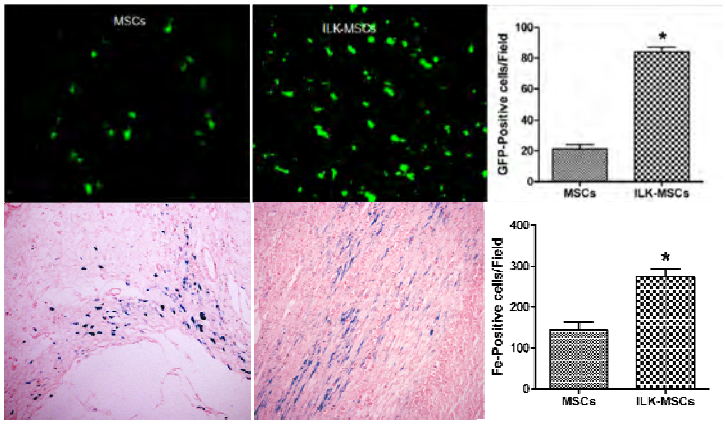


Figure2. More GFP positive and prussian blue staining positive cells is found in ILK-MSCs group two weeks later, but the degree of each cells of prussian blue staining is decreased in ILK-MSCs group.*:$p<0.001$

**Discussion:** Studies reported that the homing rate of stem cells after transplantation via vessels in patients with ischemic heart disease was less than 1% [3]. Genetic modification of stem cells with specific genes is an effective homing strategy. Previous study found that ILK gene can regulate the recruitment of EPCs to ischemic region [2]. In our study, MR molecular imaging technique was effective to in vivo track the homing, migration and distribution of MSCs labeled with USPIO. It is comfirmed by pathological findings. Our results indicate that ILK gene transfection can promote the MSCs homing to infarction region after intracoronary administration. The paradoxical MR findings that the hypointensity area and intensity variation in ILK-MSCs group were smaller/lower than those in MSCs group 2 weeks later can be explained by increased cell proliferation verified by GFP expression and prussian blue staining.

**Conclusions:** USPIO labeled MSCs can be reliably detected and tracked in vivo using serial MR molecular imaging. Transplantation of ILK-MSCs after myocardial infarction can increase the homing rate of MSCs.

**References:** [1]Janssens S, et al. Lancet 2006;367(9505):113-21. [2]Seung-Pyo L,et al.Circulation2006;114:150-9.[3]Pagani F D, et al. J Am Coll Cardiol 2003; 41(5):879－888.