Environmental Medicine, Vol. 46 No.1, 2, 2002 (page 79 ~ 80)

A New Device for Percutaneous Intramyocardial Injection of Bio-active Substances

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Abstract: Recent advances of biological treatment for diseased hearts, in particular therapeutic angiogenesis in patients after myocardial infarction, are attracting a great attention of cardiologists. The methods currently available for local delivery of various bio-active substances, however, require substantial improvement in terms of efficacy and specificity. We developed a new device for injection of therapeutic factors with high stability at the target myocardium. A practical usefulness of the device was tested in rat femoral skeletal muscle by dye injection, and its potential benefits are discussed.

Key words: new device, catheter-based myocardial injection, bio-active substances

Biological therapies are attracting a great attention of cardiologists as an innovated treatment of patients with serious heart diseases, who respond insufficiently to standard therapies using drugs, electrical devices or surgeries. For instance, therapeutic angiogenesis by application of vascular endothelial growth factor (VEGF) was successfully achieved in animal models of chronic myocardial ischemia. Feasibility of a similar approach to patients with chronic myocardial ischemia is under the investigation.[1)]

Practical usefulness of such biological therapies depends on the substance delivery system. Intravascular administration (intravenous or intracoronary) is relatively easy and safe, but suffers from low efficiency of delivery to the target tissues. Direct intramyocardial injection of angiogenic factors with open heart surgery was shown to be efficient, but the requirement for thoracotomy is a barrier to widespread application.[2)] Recently a catheter-based myocardial injection (percutaneous endocardial approach) has been exploited to achieve an efficient therapeutic angiogenesis.[3)] An improvement of the injection method for the endocardial approach would increase its usefulness in the local delivery of bio-active substances, genes, proteins or cells to diseased hearts. For this purpose, we have developed a new injection device with better stability of the needle at the target myocardium.

Methods

A retractable 27G needle, that can be protruded 3 to 5 mm, was incorporated to the distal end of a steerable and deformable 8F catheter equipped with an extractor to hold the myocardial tissue (Fig. 1). As the first step to test the feasibility of this device, we used rat femoral skeletal muscle instead of myocardium. The needle-catheter was introduced to the target site with the aid of 10F guiding catheter, and a portion of muscle was captured. Then the needle was protruded, and a small amount (0.5–2.0 ml) of dye (Evans Blue) solution was injected.

Results and Discussion

The operation of the new device was practically easy to hold the target site, and it was possible to inject precise amounts of dye solution to the muscle without distinct leakage. This was confirmed by macroscopic visual inspection (Fig. 2).

Some clinical trials of angiogenic factors using the transendocardial injection catheter have already started. Injection of VEGF gene or basic fibroblast growth factor (bFGF) protein to the ishemic myocardium was shown to have beneficial effects on left ventricle vascularization and contractive function.[4)] For such trials, one of the most popular methods using the injection catheter is the NOGA system (Biosense, Johnson & Johnson, Skillman, New Jersey, USA). It is the mapping and navigation system with the aid of 3D magnetic field and graphics computer.[5)]

To achieve the better therapeutic efficacy in abnormal myocardium, numbers of injection catheters are under development. Using the radio frequency ablation delivery system, Bao J. et al.[6)] induced bFGF protein in pig myocardium, and showed significantly higher retention of bFGF compared with previously observed for intracoronary, intravenous and intrapericardial delivery. Rezzaee M. et al.[7)] developed the helical needle drug infusion catheter, and showed it's efficacy

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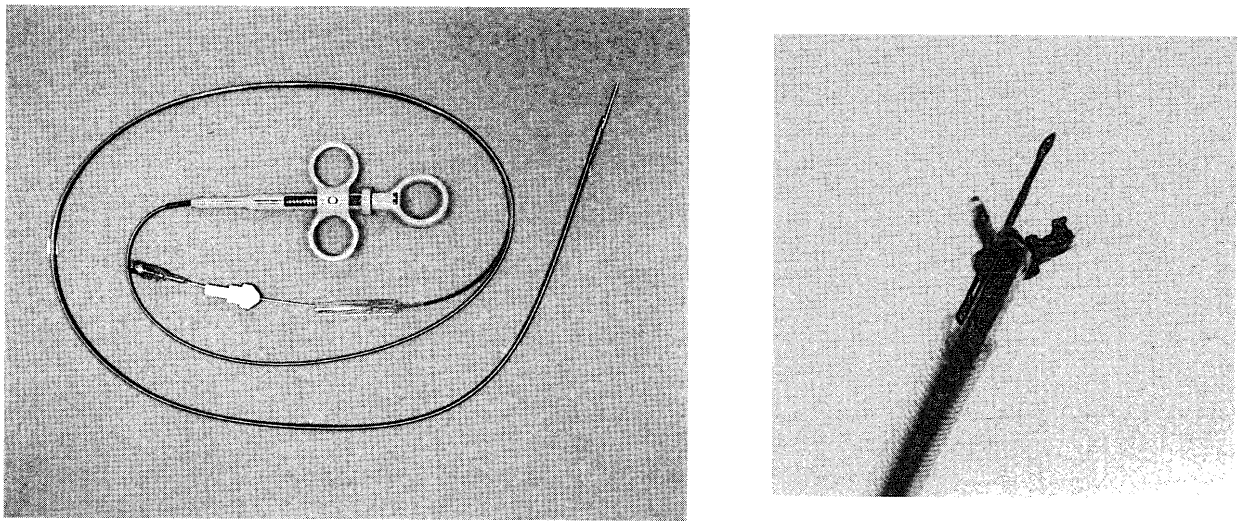

Fig. 1 The injection catheter with an extractor and a retractable 27G needle. The needle can be advanced after myocardium is caught by extractor. Bioactive substances can be injected from the syringe placed in handling side.

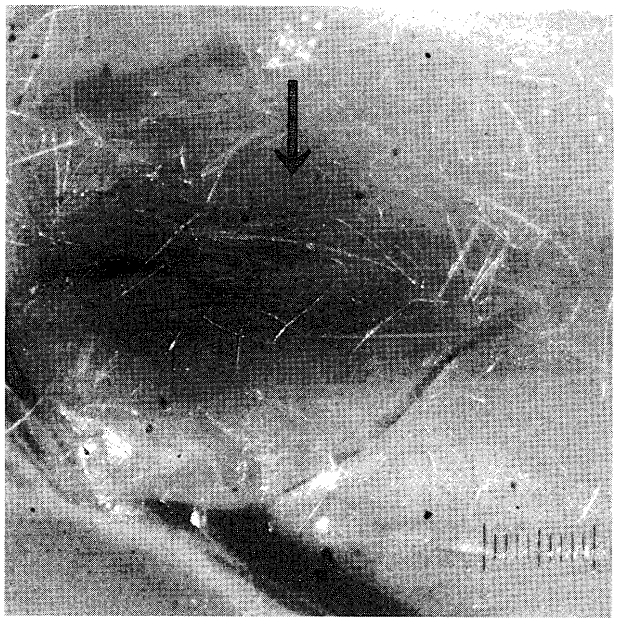

Fig. 2 Injection of 5% Evans Blue dye confirms muscle tissue staining selectively (arrow).

by injecting Iodine-labeled albumin.

Our new injection catheter with extractor has an advantage to obtain highly stable holding of the target tissue. This property would help more efficient injection of large amount or high viscosity solution.

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Received June 3, 2002; accepted June 25, 2002