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Percutaneous Intramyocardial Chemical Ablation: Preliminary Results in the Treatment of Ventricular Tachycardia Model of Dogs

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LU ET AL.: ***Percutaneous Intramyocardial Chemical Ablation: Preliminary Results in the Treatment of Ventricular Tachycardia Model of Dogs.*** *Sustained ventricular tachycardia simulated by implanted subepicardial pacing microelectrodes in 18 dogs was treated by a novel percutaneous intramyocardial chemical ablation with 100% ethanol. The ablation catheter consists of a specially designed mapping catheter and a steerable chemical ablation catheter. Ventricular tachycardia (VT) mapping and ablating manipulation was taken under the fluoroscopy in a catheterization laboratory.* ***Results:*** *The success rate of chemical ablation was 100%. The induction rate of new VT was 16.7% at 4 weeks after ablation. The acute response of VT to chemical ablation included: (1) the focus was ablated completely within 3 seconds (73.3%), and (2) VT was intermittently stopped and then disappeared within 10 seconds (26.7%). The epicardium near the ablated focus changed into pale after ethanol injection. Four weeks later, the border between lesion and normal tissue became indistinct. There were normal myocardial islands in chronic fibrous lesion.* ***Conclusions:*** *(1) It is feasible by using percutaneous intramyocardial chemical ablation to treat sustained VT. The success rate could get to 100% if VT focus is accurately mapped. (2) The ablating lesion can be limited in myocardial layer if the amount of chemical agent is appropriately controlled. The epicardium and endocardium near the lesion could be normal. (3) The induced VT after chemical ablation suggests the therapy may have potential long-term proarrhythmic effect. (J HK Coll Cardiol 2001;9:119-125)*

Catheter ablation, proarrhythmic effect, ventricular tachycardia

摘要

對 18 條狗在心外膜下置入微電極模擬持續性室性心動過速（簡稱室速）並以 100% 乙醇進行經皮心肌內化學消融，消融導管由一根特製的標測導管和一根可操縱的化學消融導管組成，標測和消融操作在心導管室 X 線透視下進行。結果：消融成功率 100%，消融後 4 周新室速的誘發率 16.7%。模型室速對消融的反應有：(1)在 3 秒內病灶完全消除（73.3%）；(2)在 10 秒內先間斷終止然後消失。消融部位的心外膜急性期呈白色，4 周後，消融灶與周圍正常心肌分界不清楚，在慢性纖維化的病灶內存在正常心肌島。結論：(1) 經皮心肌內化學消融持續性室速的方法可行；如果對室速起源點標測準確，成功率可達 100%。(2)如果消融液劑量控制恰當，可使消融病灶局限於心壁肌層，內外分別覆蓋正常心內、外膜。(3) 慢性期誘發的新室速提示這種治療方法具有潛在的致心律失常作用。

關鍵詞：導管消融　致心律失常作用　室性心動過速

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Introduction

Ventricular tachyarrhythmia is one of the most common cardiovascular disorders that influence human health and life expectancy. Refractory ventricular tachycardia (VT) causes nearly 500,000 sudden deaths per year around the world. The present therapies for malignant VT include the following:[1-4]

1. Medication: Antiarrhythmic medication has long been used as a main means in the treatment of various VTs. But it is not a radical cure. It has limited long term benefits. Certain agents may have serious side effects such as fatal proarrhythmic action.
2. ICD implantation: It is also not a radical cure. It has operative complications and requires frequent replacement in the limited years. In addition, it is expensive for patients in developing countries.
3. Open heart surgery: It complicates with high perioperative mortality, possible afteroperative arrhythmia and expensive hospitalization.
4. Intracoronary chemical ablation: It causes harmful artificial myocardial infarctions, has higher probability of proarrhythmic action and fewer indications.
5. Endomyocardial radiofrequency catheter ablation: It is more suitable to the idiopathic VT than to other ventricular tachyarrhythmias such as those complicated with ischemic heart disease. In order to explore a new interventional radical cure for sustained VT, we tested the feasibility, effectiveness and safety of the percutaneous intramyocardial chemical ablation in experimental VT model of dogs.

Material and Methods

The design and the making of the chemical ablation catheters

A special chemical catheter (Figure 1) is designed to complete the following tasks: (1) remote percutaneous manipulation in the heart; (2) precious endomyocardial mapping; and (3) accurate chemical ablation. Therefore the catheter is consisted with 2 different parts as shown in Figure 1. In briefly, one part is an outer mapping catheter and the other is an inner ablation catheter. The mapping catheter is 100 centimeters long and has one central lumen along its axis and 2 electrodes with interelectrode distance of 5 millimeters (mm) at its tip. The proximal electrode is a ring and the distal electrode is a cylinder containing a coaxial hole of 2 mm in diameter. In addition, a steerable wire is fixed at the inner wall with one end located 10 mm away from its tip. The ablation catheter is 120 centimeters long and has an inner lumen of 2 mm in diameter. At its tip is installed a micro needle with an outer diameter of 1.5 mm, an inner lumen of 1 mm in diameter and a short inclined plane of 1 mm. The needle is 5 mm long. Additionally, there are fine scales and knocking apparatus at its tail part that are used to control the needle length exceeding the tip electrode of the mapping catheter. The total lumen volume of the needle and the catheter stem is 1 ethanol milliliter. The flow capacity of the ablation catheter is 230 ul/min ethanol under 5 atmosphere pressure.

This study has been approved by the Ethic Committee of Chinese Air Force General Hospital. Mongrel dogs were provided by Chinese Military Academy of Medical Science. The subepicardial VT model has already been reported elsewhere.[5] In briefly, the dog is anaesthesed intravenously and ventilated by Bird Brand ventilator. The heart is manifested by right sternum incision and the pericardium is cut out carefully. A microelectrode of 0.5 mm by 1.0 mm is implanted as a pacing cathode in the subepicardium at the right ventricular apex under the operative microscope. The anode is a temporary needle inserted into the subcutaneous tissue of a forelimb. If the heart could be paced at 350 bpm by an appropriate diastolic threshold, then the cathode wire is properly fixed. The dog is then alive over 7 days for further ablation procedure after the pericardial and thoracic cavities are closed.

Electrophysiological Mapping and Chemical Ablation

Cardiac electrophsiological study and catheter ablation manipulation were completed in a catheterization laboratory with Philips DSA imagine system. After regular catheterization preparation, two 5F quadripolar electrode catheters (USCI Co., interelectrode distance 5 mm) were inserted via left femoral vein by Seldinger procedure to record the high

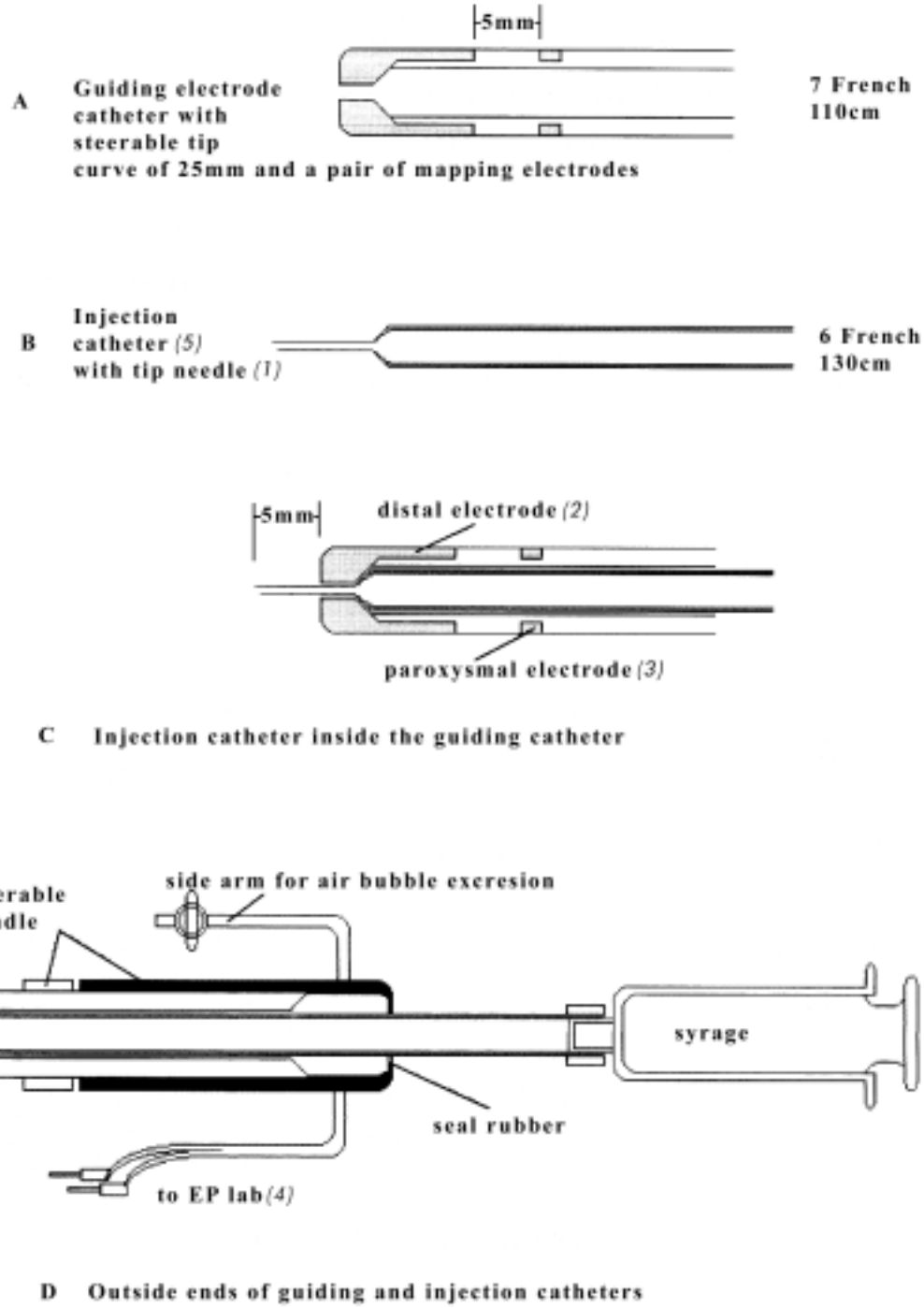


Figure 1. *The structure of the chemical catheter sets (see text for details). (1) intramural needle, (2) cylinder electrode, (3) ring electrode, (4) mapping catheter, (5) ablation catheter.*

right atrium (HRA) and the His bundle electrograms (HBE). Via right femoral vein, the chemical ablation catheter is introduced through a long shelth and positioned in right ventriculum. The surface electrocardiograms of I, aVF, V5, intracardiac HRA, HBE and the electrogram from the ablation catheter were recorded simultaneously by a RECOR (Siemens Co.). Standard cardiac electrophysiological studies were conducted before chemical ablation, 30 minutes and 4 weeks after ablation, respectively.[6,7]

After basic electrophysiological study, the VT was simulated by a cardiac programme stimulater (UHS-1, Biotronik Co.) at a pacing rate of 350 bpm and a volt of 2 times of diastolic threshold between the implanted subepicardial cathode and the subcutaneous needle anode. The mapping catheter was manipulated to map the VT focus. After that, the catheter was slightly pressed to make a stable contact between the cylinder electrode and the endocardium. The catheter was properly fixed and the electrogram was instantly monitored. Then the chemical ablation catheter was slowly screwed forward to pierce through the endocardium. The puncture depth was controlled by the tail scales. Then 2 ml ice saline solution with contrast was injected to do a trial ablation (the contrast is used to avoid possible intracoronary injection). If the VT focus was responded to the trial ablation, another 2 ml pure ethanol was injected at a speed of 200 ml/min. If the VT was ended in 10 minutes, the procedure was completed. Otherwise, more mappings and injections were taken until ablation succeeded or more than 10 milliliter ethanol was injected. After the ablation procedure, the dogs were still kept survival for another 4 weeks before an autopsy.

Data Management

Data is presented as mean±standard deviation (M±SD). Student-t test is used to analysis the data and $P<0.05$ is defined as a significant level.

Results

Subepicardial Ventricular Tachycardia Model

Altogether 18 dogs were used. Their weight was 18±3kg. Three of them were used to evaluate the implanted electrode. The other 15 were used for ablation. Three dogs among the 15 were killed after acute ablation. The other 12 were alive for more than 4 weeks for further evaluation.

All 18 implanted electrodes can be paced successfully. The pacing threshold was 0.9±0.7 volts at the time of implantation and 1.2±0.5 volts just before ablation procedure ($P<0.01$). The simulated VT was well reproduced in 4 weeks.

Acute Response of VT Focus to Chemical Ablation

Fifteen dogs with simulated VT were ablated with total success rate of 100%. Eleven of them (11/15, 73.3%) were succeeded at the first ethanol injection and VT was terminated within 3 seconds (Figure 2). The other 4 (4/15, 26.7%) succeeded at the second or third injection and VT was ended from intermittent capture to complete stop in 5-10 seconds. One dog was provoked transient couplet ventricular premature beats immediately after ethanol injection. Neither spontaneous VT nor ventricular fibrillation was observed. A small coronary imaging was observed in a dog during trial ablation. After position adjustment, successful ablation was obtained.

Chronic Response of VT Focus to Chemical Ablation

After acute ablation, 12 dogs were alive for another 4 weeks. The VT could not be simulated in 10 dogs (complete effect 10/12, 83.3%). The other 2 dogs could be simulated only intermittently (partial effect 2/12, 16.7%). Therefore the total effect rate was 100% (12/12).

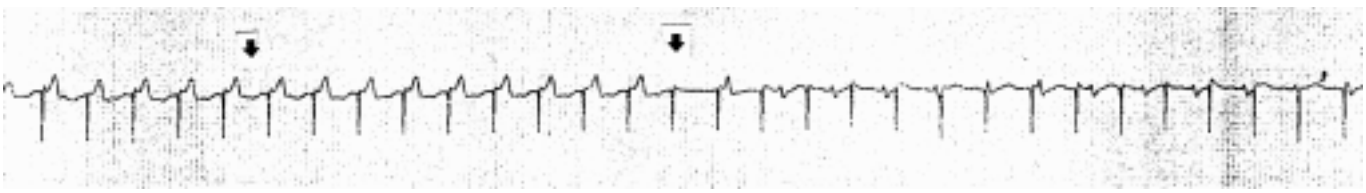


Figure 2. *The simulated ventricular tachycardia was successfully ablated within 3 seconds (second arrow) by the first ethanol injection (first arrow).*

Electrophysiological Study (Table 1)

The sinus rhythm circle length and ventricular effective refractory period were not significantly changed after chemical ablation (P>0.05). The induction rate of new sustained and nonsustained VT was respectively 5.6% (1/18) before ablation, 20% (3/15) in 30 minutes after ablation and 16.7% (2/12) in 4 weeks after ablation.

Pathological Examination

After acute ablation, the color of the epicardium above the implanted electrode became pale from its surrounding flesh red. The pale lesion was 4±3 mm in diameters with relative clear border. It was a little stiff and dyskinesis. Under the microscopy, the myocardial layer was evenly destroyed and looked like glassy change, but the epicardium and endocardium surrounding the ablation area were still integrity (Figure 3). Four weeks later, the ablation lesion focus was only seen in the middle myocardial layer. Its color changed into deep red and the lesion was completely fibrolitic with normal outer epicardium and inner endocardium. However, the border of the lesion was not so clear as that in acute stage and, occasionally, normal myocardial islands could be found in the chronic lesion.

Discussion

Methodological Evaluation

At present, although many interventional therapies of sustained ventricular tachycardia such as transcatheter direct current ablation, intracoronary chemical ablation and radiofrequency energy ablation have their series clinical reports, their drawbacks and limitations still exist. For example, transcatheter direct current ablation procedure needs general anaesthesia. Catheter disposition and serious complications are common and there are delayed proarrhythmic actions. In intracoronary chemical ablation, arrhythmic relative coronary artery is hard to be located accurately. It does not suit to ablate VT near larger coronary arteries and without appropriate relative coronary artery. Preserved heart function will be injured and new ventricular tachyarrhythmia will be provoked during or after ablation due to its artificial myocardial infarction. Radiofrequency catheter ablation now is one of the most privilege interventional means in the radical cure of VT. However, it is still not suitable to treat special VT such as their foci or reentrant loops located in subepicardium,intraseptum, intramurum and larger area of subendocardium.

Theoretically, the percutaneous intramyocardial chemical ablation approach has the advantages of: (1) radical cure, (2) little myocardial injury, (3) suitable to various intramural foci, (4) simpler procedure, (5) repeatable use, and (6) fewer complications. But actually, the above objectives are difficult to achieve because of problems such as catheter design, chemical agent selection, focus mapping, ablation manipulation and experience accumulation.

Ideal Intramural Chemical Ablation Catheter

Obviously, an ideal intramural chemical ablation catheter should have the following characters. (1) It can be easily operated by remote control. (2) It could be clearly identified under the X-ray fluoroscopy. (3) It can be used as both electrical and chemical mapping catheter without catheter exchange. (4) Both chemical and radiofrequency ablations can be conducted in compliment to each other in one procedure. (5) The

Table 1. Electrophysiological study before and after chemical ablation

	Before ablation (n18)	30 minutes after ablation (n15)	4 weeks after ablation (n12)
NSCL(ms)	302.7±57.4 (237-359)	294.1±79.5*(216-376)	315.8±43.7*(270-362)
VERP(ms)	176.3±74.6 (94-253)	184.9±96.2*(87-218)	168.6±84.3*(82-254)
VTs	1	1	0
VTn	0	2	2

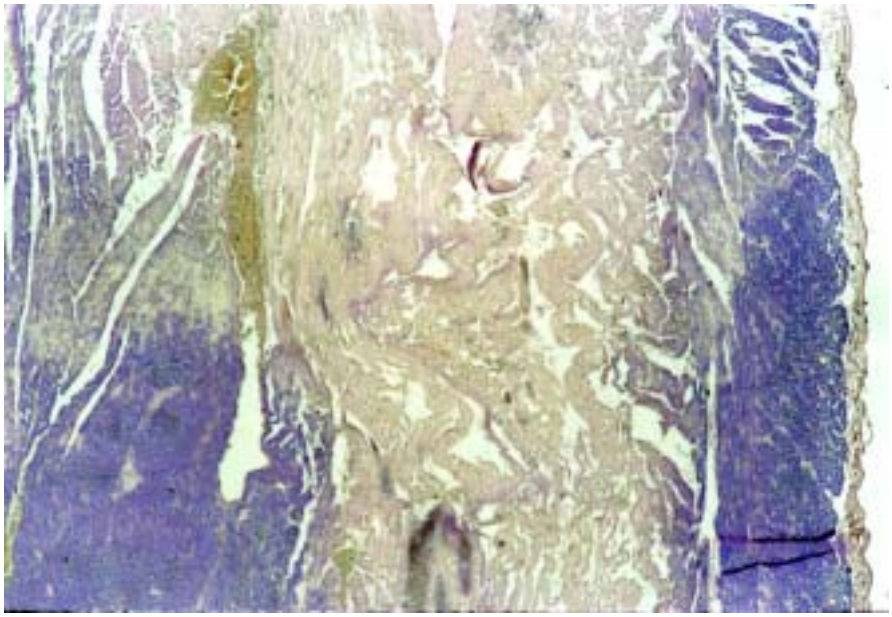
* P>0.05 when compared with before ablation

NSCL: normal sinus circle length

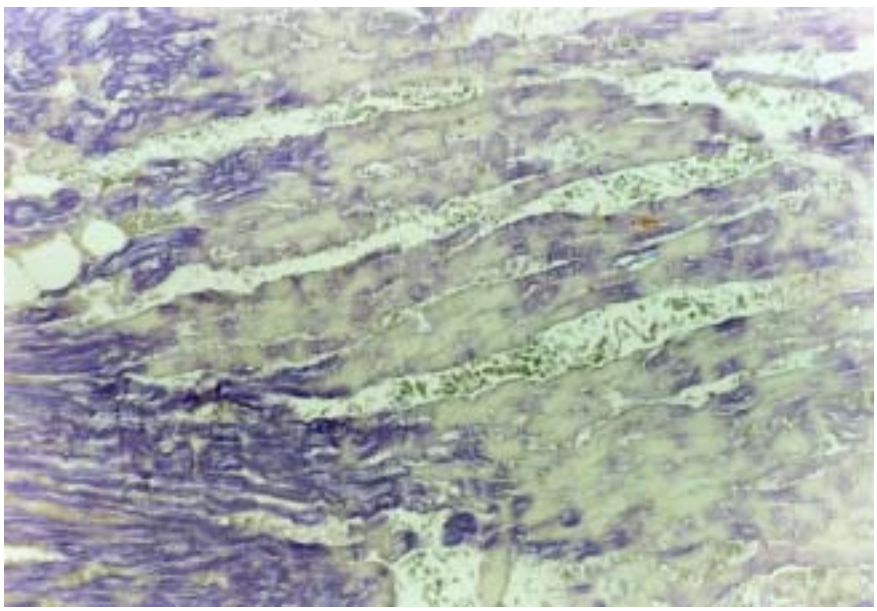
VERP: ventricular effective refractory period

VTs: sustained VT

VTn: nonsustained VT



(A)



(B)

Figure 3. *Myocardial pathology after chemical ablation with 100% ethanol. (A) In the ablation area, the myocardial layer was evenly destroyed and looked like glassy change. The endocardium was still integrity. (B) The border between ablation target and normal area was distinct.*

injection volume and velocity of chemical agent can be preciously selected. (6) Intramural electrical activity can be mapped simultaneously with other electrograms by microelectrodes installed in the injection needle. All these characteristics are very important for safer and more effective intramural chemical ablations. The catheter used in this study obviously did not include all above characters.

Ventricular Tachycardia Model for Interventional Electrophysiology

The commonly used animal model of VT includes: (1) coronary ligation and artificial myocardial infarction; (2) chemical agent injection in coronary artery, coronary vein, or peripheral veins to injure myocardium and form irregular focus; (3) intramural chemical agent injection to produce irregular excitement

focus. The disadvantages of these models are: (1) low VT production rate; (2) low reproducibility rate; (3) high false positive and false negative rate; (4) limited selection of VT original position, number, morphology and type; (5) not suitable to evaluate the effect of interventional treatment.

The new VT model in this study has the following characters: (1) higher production rate and less material waste; (2) higher selection and less randomization; (3) more stable and reproducible; (4) various VTs can be simulated; (5) can be used to both acute and chronic experiment.

Effect Evaluation of Intramural Chemical Ablation

In this study, all 15 dogs were ablated successfully. This result is obviously related to focus mapping accuracy because the preimplanted microelectrode could direct the precious and effective endomyocardial mapping under fluoroscopy. Therefore, if this technique is used in practice, accurate target area mapping will be the key point.

Pathological Characters of Intramural Chemical Ablation

After intramural chemical ablation, the epicardium and endocardium structure is still intact. Although it is not sure whether these structures participate in long term proarrhythmic actions or not, it is no doubt that they are very important to maintain the regional systolic and diastolic functions. In addition, the induction rate of the new VT is 20% in 30 minutes after ablation and 16.7% in 4 weeks after ablation respectively. They are significantly higher than that of the preablation (5.6%). This strongly suggests that the remained pathological changes after ablation are proarrhythmogenic. It is supported by the evidences that the border of the ablation lesion is not distinct from the surrounding normal tissues and the alive myocardial islands in region with chronic fibrous changes. This action is due to the chemical agent selected or the ablation lesion itself needs to be further evaluated.

Limitation

(1) The VT model used in this study is a focal mechanism. It is very different in characters from the VT originated from the previous myocardial infarction. Therefore, an ischemic VT model is needed to test the feasibility and effect of this chemical ablation procedure. Otherwise, In this focal VT model, a sutured epicardial pacing microelectrode was used. This electrode can be used as a marker to induce the ablation and mapping catheter manipulation under fluoroscopy. It will make the ablation procedure easier than the natural VT ablation. (2) The VT chemical ablation was tested only in right ventricle. In the majority of patients with ischemic VT, the sites of VT are usually originated from the left ventricle. Therefore, further experiments are needed to study the mapping and ablating effect of the chemical ablation in the left ventricular originated VT.

Summary

Percutaneous intramyocardial chemical ablation conducted by a specially designed chemical ablation catheter is feasible in the treatment of sustained focal VT. The success rate could be 100% if the VT focus is accurately mapped. No serious complications are found. The ablation lesion is limited only in the myocardial layer with intact epicardium and endocardium. Therefore, the heart function is not influenced. New VT induced after ablation suggests the potential long term proarrhythmic action.

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